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THE ANGIOGRAPHIC STUDY OF CAROTID INSUFFICIENCY AND CEREBRAL ISCHEMIA*

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DEATH and disablement caused by cerebrovascular disease are major medical problems confronting the profession today. The living invalids afflicted by this group of diseases outnumber persons made invalid by malignancy and constitute a tremendous loss to the country.

Usually "strokes" have been considered to be the result of intracerebral infarction or thrombosis, the treatment of which is usually supportive in the hope that survival and possibly some return of function will occur. It is now quite evident that many of these patients are actually victims of thrombosis or stenosis of the cervical carotid artery. Early correct diagnosis, as afforded by angiography, now makes possible the development of a successful surgical attack.

Interest in this problem was awakened and stimulated by Fisher's[5] arresting paper on the autopsy findings of carotid stenosis and thrombosis at McGill University. Although this is by no means a new concept, there was previously little appreciation of the frequency of occurrence of this condition.

Until early in 1956, we routinely visualized only the cerebral vessels and those of the upper neck, as is usually done in most clinics. When cerebral vessels did not fill or if constriction of the cervical carotid artery was specifically suspected, a special roentgenogram of the low neck area was made in addition. We then modified our apparatus so that the cervical carotid artery, below the bifurcation, was routinely seen in every case examined. After this change we encountered a surprisingly high incidence of stenosis just distal to the bifurcation—significant stenosis was observed six times as often as complete occlusion. Furthermore, several patients with considerable narrowing of the internal carotid artery later came in with occlusion and severe brain damage, convincing us that the best chance of preventing cerebral catastrophe lay in surgical intervention before the final complete occlusion occurred. Following the occurrence of complete occlusion, surgery is often doomed to failure by intracranial extension of the clot or embolization to small branches.

As experience increased, it became evi-

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dent that symptoms were so protean and so frequently resembled other brain lesions such as tumor, hemorrhage, psychosis, and others that clinical appreciation was frequently impossible. The so-called clinical symptoms of carotid thrombosis are unreliable. Although other diagnostic methods, such as carotid compression and ophthalmodynamometry, are suggestive and helpful, angiography with routine inclusion of most of the cervical carotid artery is the only true diagnostic procedure. In our institution angiography is done as an emergency procedure whenever indicated and has proved very safe.

HISTORICAL BACKGROUND

The syndrome of spontaneous artery stenosis and occlusions as a result of atheromatous plaques in the area of the carotid sinus was first described by Chiari[1] in 1905. In 1914, Hunt again emphasized the role of the carotid arteries in producing lesions of the brain and urged their routine examination at autopsy.

The precise antemortem diagnosis became possible in 1937 when Egas Moniz[2,3] first described the use of cerebral angiography. He reported 4 cases of cervical occlusions of the carotid artery demonstrated by angiography. Numerous case reports followed largely from the European clinics. Hultquist[7] in 1942 reported 91 cases of cervical carotid artery occlusion in 3,500 autopsies.

Johnson and Walker[9] found 10 reported cases and added 6 cases of their own in 1951. It is interesting that until 1951 only 17 clinical cases were reported in the American literature and 84 cases in the European literature. Then in 1952 Fisher of McGill University reported finding carotid thrombosis or severe stenosis present in 9.5 per cent of 432 unselected autopsies and in 20 per cent of cases of cerebrovascular disease. This amazingly high incidence was found only when neck dissections were routinely done, a procedure not generally followed in performing an autopsy. Forty-five carotid artery occlusions or severe stenosis were seen, while cerebral embolism from all causes was present only 55 times and intracerebral hemorrhage only 32 times. Furthermore, Fisher called attention to the marked ischemia that occurs with any appreciable stenosis. Flow through a tube varies as the fourth power of the radius (Bernoullis' theorem).

Many more cases have since been added to the literature including reports of Webster, Gurdjian and associates,[17] but the emphasis has been on those showing either complete occlusion or extremely severe stenosis—practically complete occlusion. Much can be learned from studying those people with lesser degrees of stenosis and when possible it is desirable that treatment be undertaken at this earlier stage.

MATERIAL STUDIED

In our department 1,535 cerebral angiographies were made between January, 1951 and May, 1958. From 1951 through 1954 the principal emphasis was on the diagnosis of aneurysm, tumors, arteriovenous malformation, etc. One case of carotid thrombosis was diagnosed in 1954. In several additional angiographies, filling of intracerebral circulation was not obtained, but at the time of injection this was attributed to faulty technique.

By April, 1955 material improvement had been made in injection and roentgenographic techniques, and an improved contrast medium (hypaque sodium 50 per cent) was in use. Furthermore, it was felt that the procedure could be safely performed on the patient with an acute cerebrovascular accident. An additional injection and separate roentgenograms of the neck area were made whenever it was felt to be so indicated.

From April 22, 1955 to March 3, 1957, 524 angiographies were made. Table 1 gives the diagnoses, other than normal, established by those studies.

In March, 1957 alterations in the equipment made it possible to routinely include the neck down to the sixth or seventh cervical vertebra on all studies. In the last

Table I

INCIDENCE OF LESIONS FOUND IN 524 ANGIOGRAMS FROM APRIL 22, 1955 TO MARCH 3, 1957

	No. of Cases
Thrombosis of internal carotid artery	18
Thrombosis of vertebral artery	2
Thrombosis of anterior cerebral artery	3
Thrombosis of middle cerebral artery	4
Significant stenosis of carotid artery	10
Tumor	33
Aneurysm	20
Subdural hematoma	3
Arteriovenous anomaly (shunts, hemangiomata)	9
Intracerebral hemorrhage	1
Hydrocephalus	2
Aneurysmal dilatation of carotid siphon	3

626 angiographies performed on 482 patients, the bifurcation of the common carotid was routinely viewed in every case. We feel that including the carotid bifurcation in every case is essential. Table II gives the diagnoses made in this series.

This latter group of cases is more significant because the arteriosclerotic lesions of the carotid arteries were adequately studied even though the patient was being examined for suspected intracranial lesions. The much greater incidence of stenosis diagnosed in the second group was not only due to the routine inclusion of the neck but to the higher index of suspicion of the clinicians as well.

Of those patients showing occlusive disease 91 were male and 38 female. The average age of the males was sixty-three years and the females fifty-five years. The youngest male in which an arteriosclerotic stenosing plaque was seen was thirty-one years old and the youngest female was thirty-five. The younger age of the females in the group seemed a little surprising as serious arteriosclerotic disease elsewhere generally is thought to occur at a later period in women.

The youngest patient with complete arteriosclerotic occlusion of the internal carotid was forty-five years of age. One case from the earlier group occurred in a seventeen year old boy as a result of trauma. While participating in an amateur prize fight his face and neck were struck many times; hemorrhage into the vessel wall near the carotid bifurcation resulted in thrombosis of the internal carotid artery. He was comatose for two days before being brought to the hospital. The obstruction of the carotid artery was removed, and he recovered consciousness but continued hemiplegic. A repeat angiogram revealed occlusion of the middle cerebral artery. All other cases reported herein had arteriosclerotic occlusive disease. This boy, however, illustrated one of the oft recurring problems in treatment. If any prolonged period has elapsed between the catastrophic occlusion and operation, ascending thrombosis and/or emboli may have occluded the middle or anterior cerebral artery. If the carotid siphon does not fill by ophthalmic collateral flow, as it did not in this case, such a complication should be strongly suspected. These cases must be examined, diagnosed, and treated as acute surgical emergencies.

Table II

INCIDENCE OF LESIONS FOUND IN 626 ANGIOGRAMS MADE OF 482 PATIENTS SINCE MARCH, 1957 (CAROTID BIFURCATION ROUTINELY INCLUDED IN THE ANGIOGRAPHIES)

	No. of Cases
Thrombosis of internal carotid artery	21
Thrombosis of anterior cerebral artery	7
Thrombosis of middle cerebral artery	9
Stenosis of carotid artery	108
High grade stenosis (60 per cent or more)	33
Moderate stenosis (30 per cent or more)	30
Mild stenosis (less than 30 per cent)	45
Stenosis of anterior cerebral artery	9
Stenosis of middle cerebral artery	2
Tumor	58
Aneurysm	35
Subdural hematoma	2
Arteriovenous anomaly	11
Intracerebral hemorrhage	3
Abscess	1

FIG. 1. Complete occlusion of the internal carotid artery at the bifurcation with collateral siphon filling via the ophthalmic artery.

Figure 1 illustrates a complete occlusion of the internal carotid artery at the bifurcation, the site in two-thirds of such complete occlusions.[5] Figures 2, 3, 4 and 5 show severe, moderate and mild degrees of stenosis.

CLINICAL FEATURES OF CAROTID THROMBOSIS AND STENOSIS

The so-called "classic" clinical syndrome of carotid thrombosis is (1) monocular optic atrophy and blindness and (2) contralateral hemiplegia. Actually none of our cases satisfied these criteria completely. In over 100 autopsy cases, Ralph[12] reported that the classic concept was present in only 10 per cent. Obviously, these diagnostic criteria alone are of little use in the selection of cases for treatment.

Symptoms vary widely depending on the extent of the block, the rapidity of the onset and the effectiveness of the collateral circulation. Because of the prolonged period during which increasing stenosis occurs, some collateral circulation develops, though, at best, it is only fair in the cerebral circulation when compared to collaterals that develop elsewhere in the body.

Four principal pathways of collateral blood flow have been clearly established in angiograms.[13,16] They are: (1) from the opposite internal carotid artery through the circle of Willis; (2) from the external carotid artery on the same side into the ophthalmic artery via several routes; (3) from the external carotid artery into the vertebral system; and (4) from the vertebral system through the circle of Willis.

Visualization of the ophthalmic artery is extremely common. It was identified in all but 2 of the carotid stenoses studied; and, when complete occlusion in the neck was present, limited filling of the siphon through the dilated ophthalmic artery was often seen (Fig. 1). In fact, this is extremely important in the selection of cases for endarterectomy. If the siphon is not seen, the

FIG. 2. Severe stenosis of the internal carotid artery in the neck (short segment type). Also stenosis in the siphon.

chances of achieving patency of the vessel are very poor, as the siphon and/or cerebral vessels are probably thrombosed.

Cross circulation from the opposite carotid artery is seen with some regularity and occasionally is very copious (Fig. 6 and 7). The patient illustrated experienced an episode of hemiparesis two years before admission from which he recovered. He later developed varying symptoms of transient bilateral weakness, mental disturbances, and speech loss as the progressive stenosis in the internal carotid became more severe.

Collateral circulation from the vertebral system has often been seen in carotid block (Fig. 8, *A* and *B;* and 9, *A* and *B*).

The recognition of gradually appearing symptoms over months to years is extremely important, for these provide the early warning signs during a period when diagnosis and successful treatment is pos-

Fig. 4. Moderate stenosis of the internal carotid artery in the neck of a thirty-five year old female.

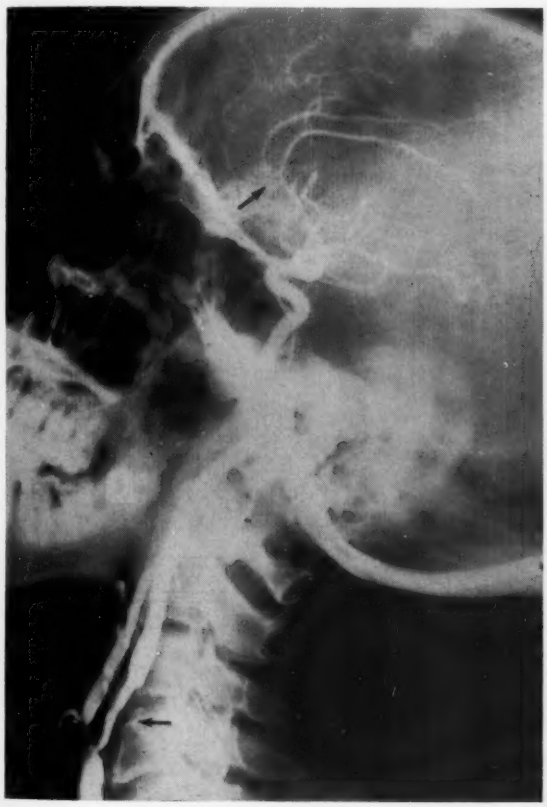

Fig. 3. Severe stenosis of the internal carotid artery in the neck (long segment type). This type is less amenable to endarterectomy.

Fig. 5. Minimal stenosis of the internal carotid artery in the neck of a fifty-nine year old male.

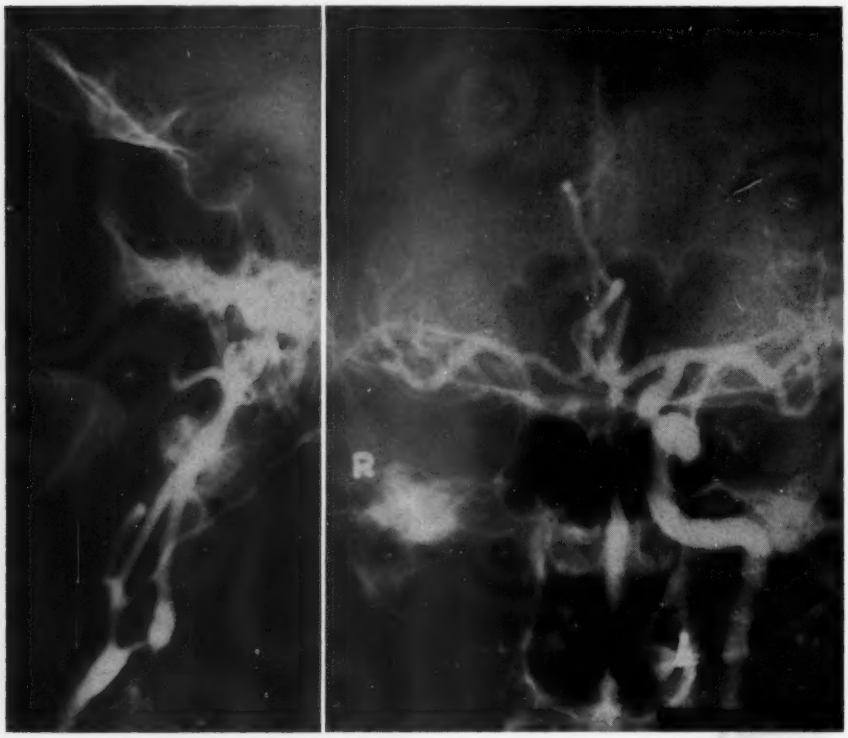

FIG. 6. Severe stenosis with excellent collateral filling from the opposite carotid artery via the circle of Willis.

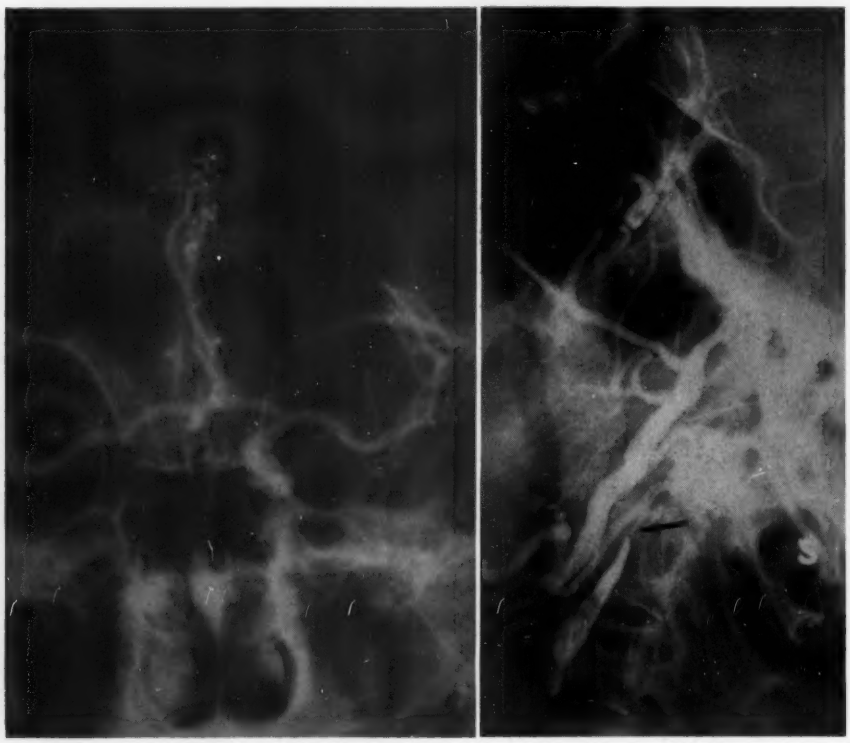

FIG. 7. Complete occlusion in the carotid siphon with the typical pointed, slowly advancing, column of medium in the neck. Excellent cross-filling from the opposite side.

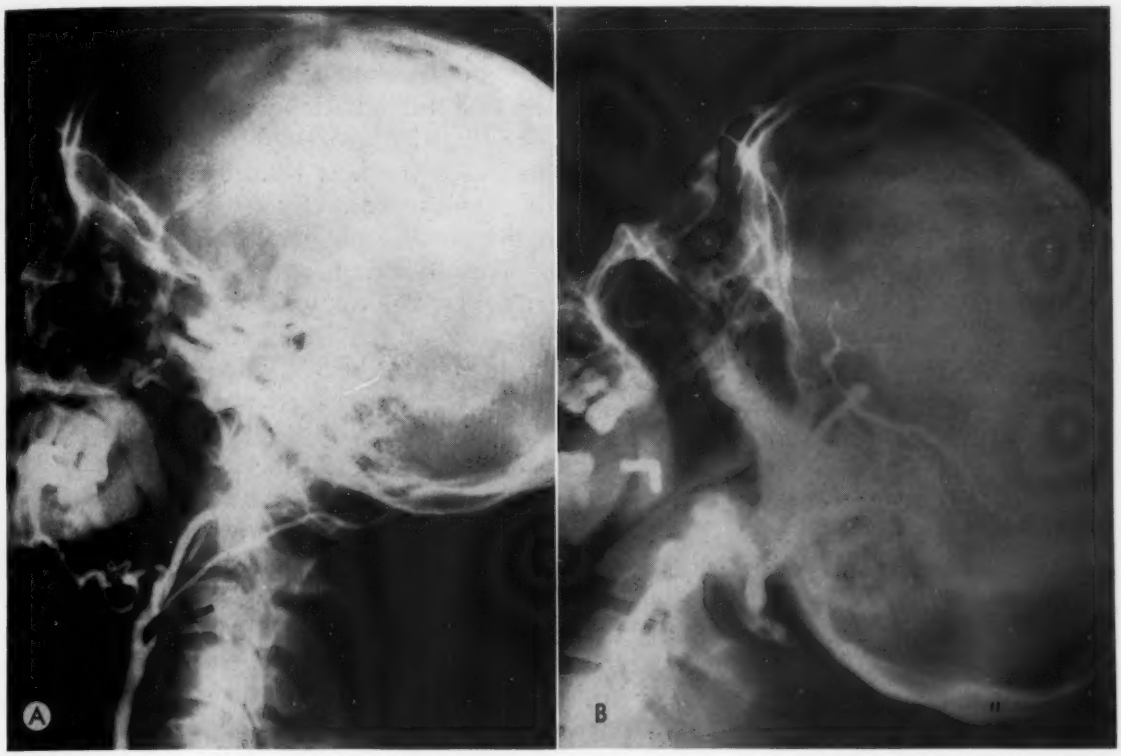

Fig. 8. (*A* and *B*) Internal carotid occlusion in the neck with collateral filling of the middle cerebral artery via the vertebral and basilar arteries.

Fig. 9. (*A* and *B*) Severe stenosis of left internal carotid artery with anterior and middle cerebral arteries filling on both sides via the vertebral and basal arteries. Patient also had complete occlusion of right internal carotid in the neck. The left internal carotid was successfully operated upon.

sible. The onset of transient symptoms, usually vertigo, headache, personality changes, hemianopsia, speech difficulties, and weakness preceded the final catastrophic occlusion by more than four years in one case. All patients with high grade stenosis of the internal carotid artery (a reduction in the diameter of the vessel of 60 per cent or more) presented symptoms. A considerable number of those patients classified as having "moderate" stenosis presented symptoms. None with "minimal" stenosis had related symptoms. In most of the cases of arteriosclerotic occlusion reported herein, it was possible, on reviewing the history, to establish a prodromal period. Angiography may some day be performed on all patients with these vague symptoms, as these are the "golden days."

Prognosis in the natural course of complete occlusion is forbidding, with 75 per cent of the patients going progressively into hemiplegia, hemianesthesia, mental deterioration, and death.

The major symptoms that we have observed in carotid insufficiency are given with their general frequency of occurrence in Table III. The type of symptoms seen in moderate to severe stenosis is much the same as those found in complete carotid occlusions; only the severity varies. At times, because of a well developed collateral circulation, symptoms following complete occlusion are surprisingly vague.

It should be especially stressed that usually patients with moderate stenosis and all patients with severe stenosis have some combinations of these symptoms. However, since findings are indefinite, symptoms often evanescent and mild, and spinal fluid normal, these patients are most frequently considered neurotics. Yet this is the group in which the best results can be obtained if they are correctly diagnosed. They deserve carotid angiography.

TABLE III

SYMPTOMS IN CAROTID INSUFFICIENCY

	Per Cent
Muscular loss, varying extent, often transient	80
Speech disturbances	60
Headache	50
Eye changes, all types, all degrees of severity	25
Paresthesias	20
Convulsions	20
Mental disturbances	15

We are convinced that cerebral angiography, as currently performed, is safe and, in view of the invaluable information it yields, should be freely done on all types of cases when an experienced team is available. Rowbotham *et al.*[14] and List[10] consider recent thrombosis, embolism, advanced hypertension, and arteriosclerosis contraindications for arteriography. We have not found this to be true. We have done many examinations on patients in all of these categories and in 1,535 patients only 3 developed transient hemiplegia during the examination. These later cleared completely. There were no deaths unequivocally attributable to the studies. Two patients who had occlusions, one of the carotid artery and one of the basilar artery, died within twenty-four hours. However, their condition was deteriorating rapidly before examination and continued to decline to death. One patient with a bleeding aneurysm died within twenty-four hours. Angiography may have contributed to this death.

Shapiro and Peyton,[15] Ralph,[12] James,[8] and others[4,6,18] have specifically recommended doing angiography on the patient with an acute cerebrovascular accident. Accurate evaluation of the danger of angiography in vascular lesions alone is difficult to obtain from the literature, as all series include various types of lesions. However, mortality should be extremely low and nonfatal complications less than 2 per cent if care is taken. The last 1,150 of our examinations were made with hypaque sodium 50 per cent, a contrast medium that has proved safe and yields excellent roentgenograms with a 5 to 7 cc. injection. We believe that it is important to use the percutaneous method, a small injection mass,

and no compression of the surrounding vessels. The normal volume flow of a vessel should never be greatly exceeded during injection for angiography. (This principle applies to all types of arterial studies including cardioangiography.) Since the stroke volume of the carotid artery is about 3.5 cc., the injection of 7 cc. in approximately one and one-half seconds is a safe injection mass and forcing in a larger mass of material rapidly may account for some of the reported serious accidents.

PATHOLOGY

The etiology of carotid stenosis and its consequent thrombosis is arteriosclerosis in all but an occasional case. Rarely tumor, trauma or embolism may produce it directly. It is not possible to consider the general problem of arteriosclerosis; however, several worthwhile observations, not generally appreciated, can be made by studying the angiogram. With the exception of Fisher's findings, autopsy studies have contributed very little of value to our knowledge of this problem in recent years; but clinical studies, especially angiography, are expanding our knowledge rapidly.

There are 4 clinical and pathologic entities apparent: (1) solitary constriction at the bifurcation of the common carotid artery; (2) localized constriction in the carotid siphon or in the anterior or middle cerebral arteries (Fig. 10; 11, *A* and *B;* and 12); (3) multiple small plaques in secondary and tertiary cerebral arterial branches; and (4) uniformly narrow, sparse vessels throughout the brain without any definite identifiable plaques.

The first two entities occur in a relatively young age group, usually go to complete occlusion, and often show disease in only one area. The third entity (Fig. 13) is commonly seen in a much older patient who typically develops senile mental changes and perhaps, very late, an intracerebral hemorrhage. While patchy, the disease is generalized. The fourth entity (Fig. 14) is

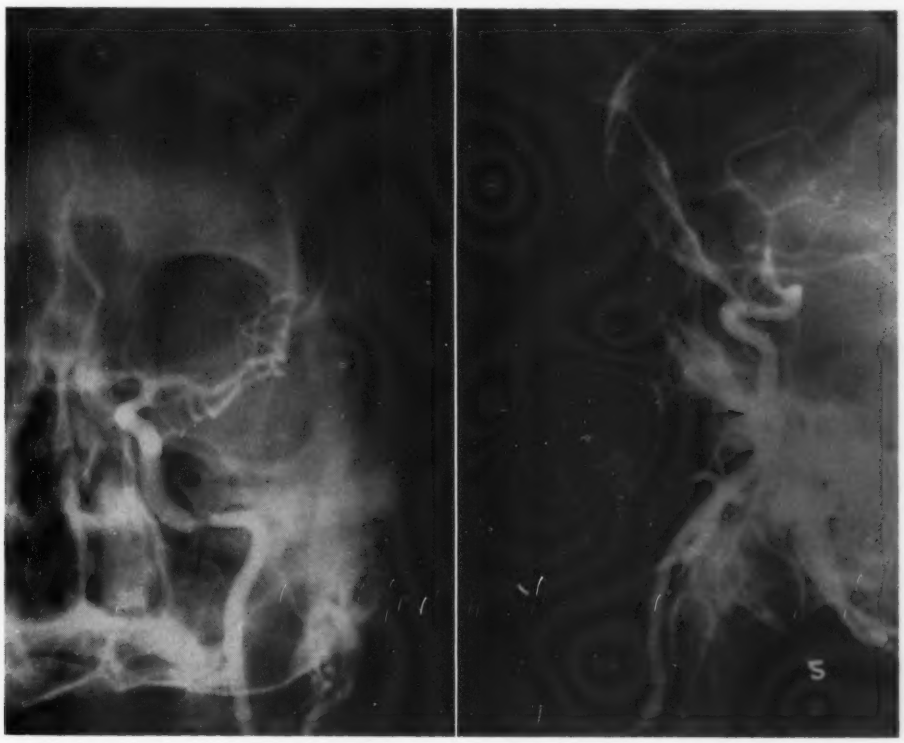

Fig. 10. Short segment stenosis in the carotid canal, a very unusual site. Visible only in the anteroposterior view.

Fig. 11. (*A* and *B*) Complete occlusion of the anterior cerebral artery.

a peculiar process, the etiology of which is not understood. It is seen in association with cerebral atrophy and its appearance is somewhat similar to Berger's disease and periarteritis nodosa as shown on femoral angiograms.

Trauma would seem to play a role in the common occurrence of carotid occlusive disease at the bifurcation. An elongated, looped or redundant carotid artery

Fig. 12. Complete occlusion of the middle cerebral artery.

Fig. 13. Multiple stenoses of major branches of the anterior and middle cerebral arteries. These are usually seen in the older patient and are typically associated with senile dementia.

Fig. 14. Generalized uniform wire-like narrowing of all intracerebral vessels. This type of narrowing is thought to precede brain atrophy.

has been seen frequently in our series of angiograms, and we have never observed stenosis or thrombosis in the cervical carotid artery in any of these patients. Therefore, it seems logical to assume that trauma to the area of the bifurcation by its constantly being pinned against the spine by overlying neck muscles is an important etiologic factor. Eddy currents at a bifurcation are probably another factor.

Another apparent consequence of carotid stenosis has been noted—the frequent association of carotid or cerebral stenosis and cerebral atrophy. Atrophy is the most common condition diagnosed by pneumoencephalography, and the concomitant occurrence of atrophy and stenosing plaques has been observed repeatedly. If on further study this proves to be a close relationship, the importance of diagnosing and treating stenosis may be even more significant. We have seen atrophy associated with all of the various types of stenosing disease described earlier (Fig. 15, *A*, *B* and *C*; and 16, *A* and *B*).

TREATMENT OF CAROTID THROMBOSIS

Two-thirds or more of all occlusions of the internal carotid artery start at the bifurcation in the neck and only one-third occur intracranially;[5,9] therefore, the majority are quite accessible surgically.

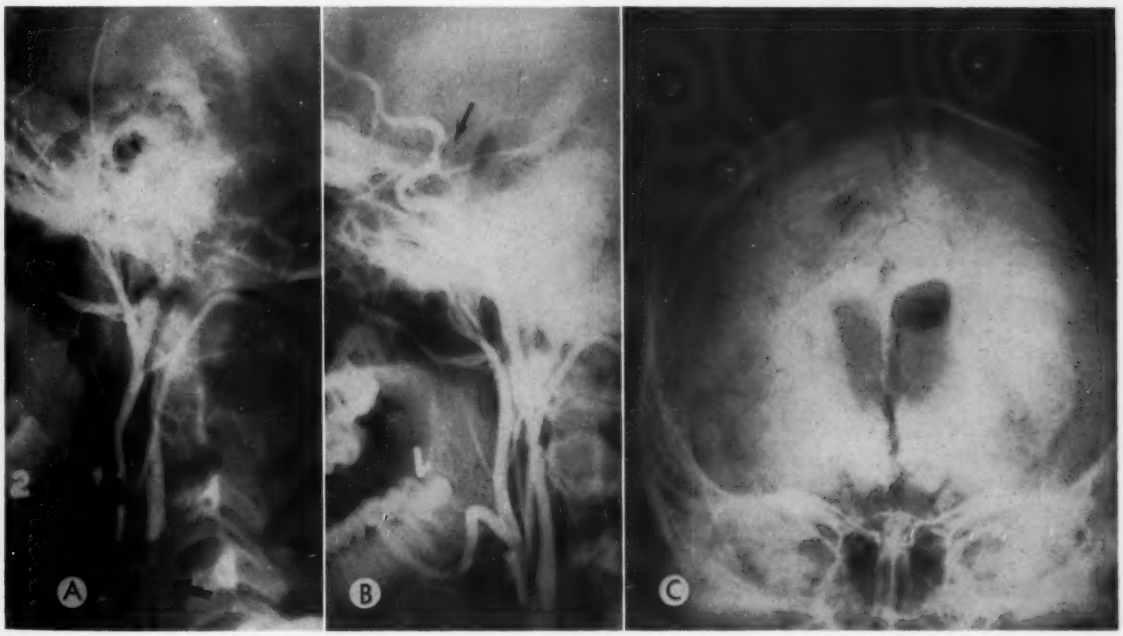

Fig. 15. (*A*, *B* and *C*) Traumatic occlusion of the internal carotid artery in the neck of a sixteen year old boy. Ascending thrombosis into the cranium. Endarterectomy with clot removal and restoration of carotid flow, but thrombosis of middle cerebral artery and continued hemiparesis. Hemiatrophy visible in ten days.

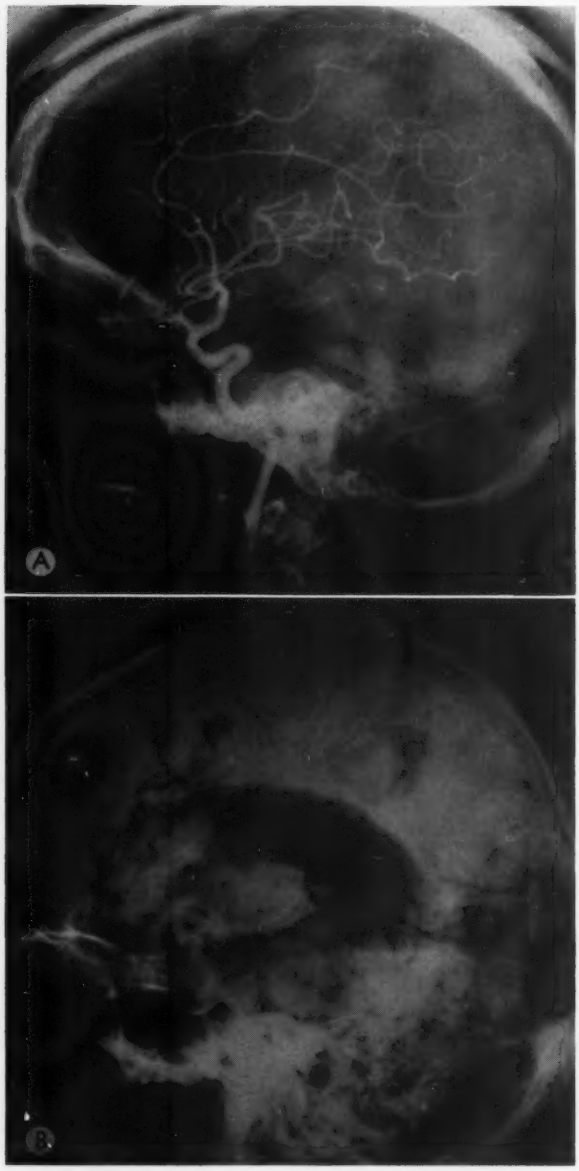

FIG. 16. (*A* and *B*) Generalized uniform wire-like constriction of all intracerebral vessels with advanced atrophy.

In the past, a few cases have been treated by one of the following procedures: (1) stellate block or sympathectomy; (2) arterial stripping; (3) excision of the thrombosed vascular segment to prevent spasm; (4) ligation of the carotid siphon intracranially to prevent emboli; (5) anticoagulants; and (6) endarterectomy. Only the last two procedures have proved to be of any great value. Anticoagulants will prevent the thrombus from propagating from the neck up into the anterior and middle cerebral artery, but must be continued indefinitely, and *do not in any way improve the cerebral ischemia*, the major problem.

Surgical relief of the occlusive disease has been attempted on 28 of our patients. Murphey, Schultz and DeSaussure[11] explored or performed endarterectomies on 32 cervical carotid arteries in these 28 patients. Nineteen vessels were operated upon for complete occlusion and 13 for moderate or severe stenosis. In most cases there was bilateral involvement of neck vessels to some extent, and in 10 patients there was serious vascular constriction on both sides. In 2 patients both internal carotid arteries were completely occluded. These patients were surviving only on collateral circulation by way of the vertebral arteries. One of these was endarterectomized bilaterally and experienced a dramatic return of function. Table IV gives the distribution of severe occlusive disease in these 28 patients.

In the operated group 24 were males with an average age of fifty-eight years, and 4 were females averaging sixty-two years of age. The youngest woman was forty-two years old and the youngest man forty-seven years. The seventeen year old boxer who suffered a traumatic occlusion as described earlier is included in this group.

In all of the above cases endarterectomy was carried out or attempted; no permanent bypass grafts were inserted. In all cases except 4, anticoagulants were used for

TABLE IV

DISTRIBUTION OF SEVERE OCCLUSIVE DISEASE IN 28 PATIENTS OPERATED UPON

	No. of Cases
Complete occlusion of one side	11
Severe stenosis (60 per cent or more) of one side	7
Severe stenosis of one side; complete occlusion of the other side	7
Severe bilateral stenosis	1
Complete bilateral occlusion	2

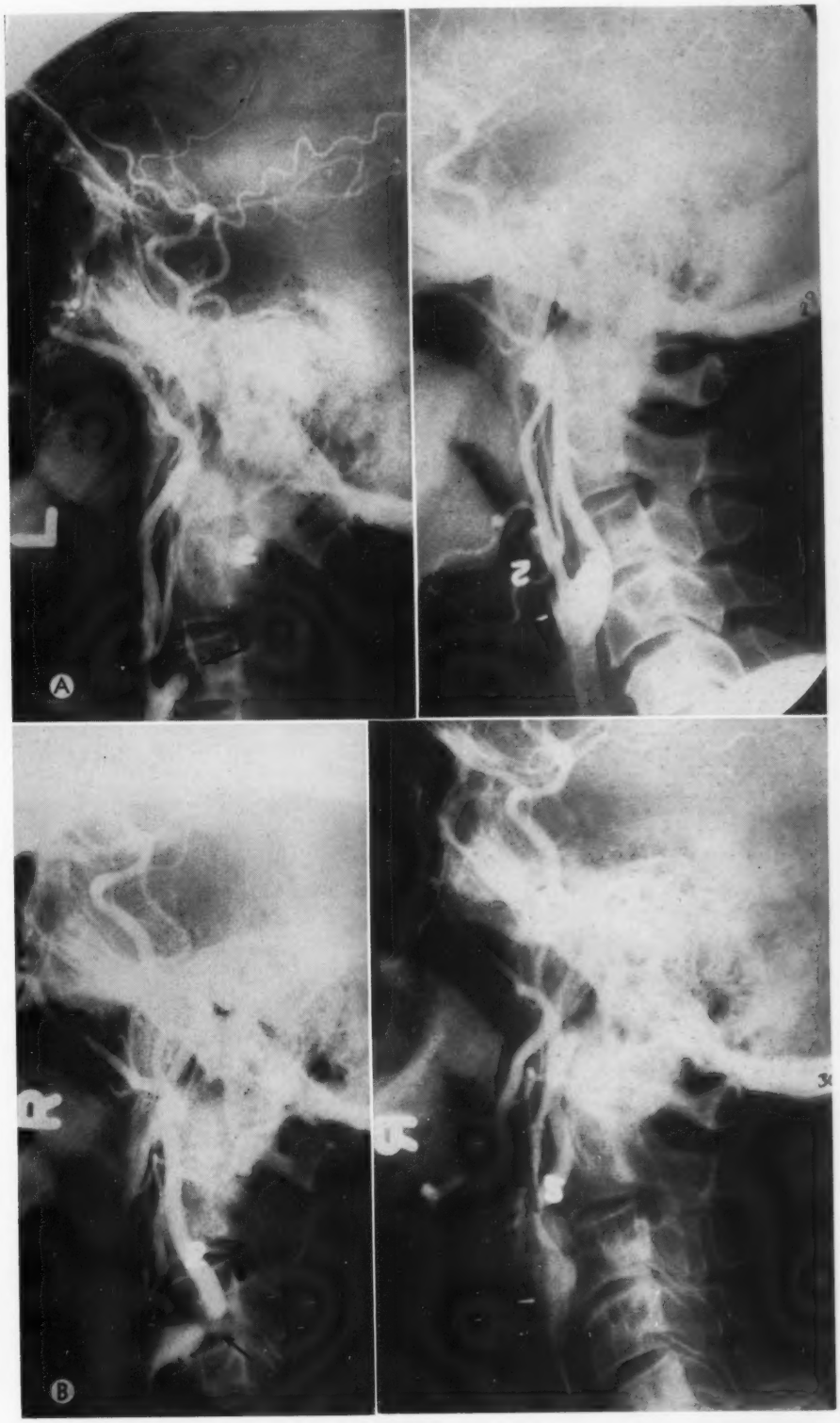

Fig. 17. (*A* and *B*) Fifty year old male with complete occlusion of the left internal carotid artery. Left endarterectomy was performed with good return of flow but with residual occlusion of ascending frontoparietal artery and continued partial hemiparesis. This patient also presented severe stenosis on the right. Right endarterectomy was performed with good return of flow.

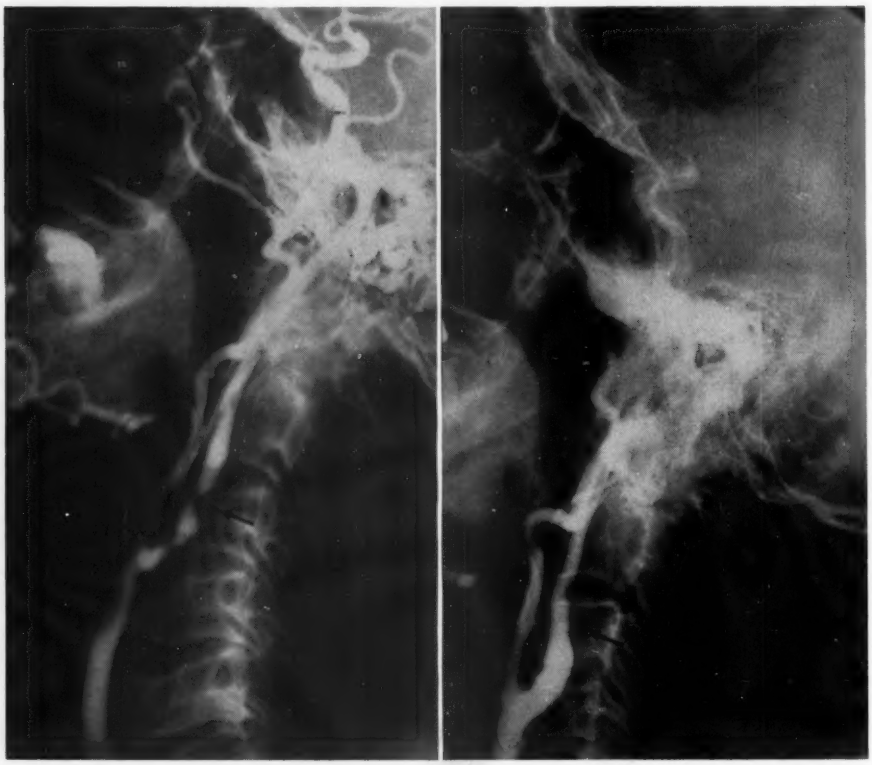

FIG. 18. Fifty-nine year old male with severe stenosis of internal carotid artery on the left and old complete occlusion on the right. Left endarterectomy was performed with marked clinical improvement.

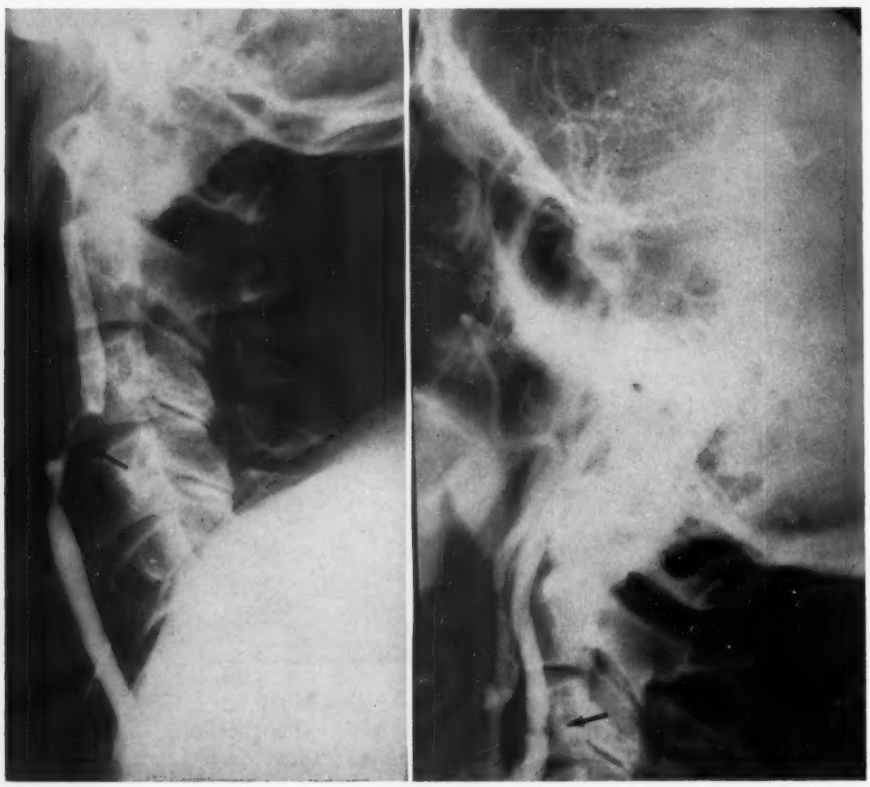

FIG. 19. Fifty-eight year old male with severe stenosis of the left internal carotid artery and mild stenosis of the right. Left endarterectomy was performed, followed by marked clinical improvement.

Table V

RESULTS OF ENDARTERECTOMY ON 32 CAROTID ARTERIES IN 28 PATIENTS

Complete occlusions	
Patency not restored	9
Patency restored, no clinical improvement	6
Patency restored, good result	4
Patency restored, excellent result	none
Severe stenosis	
Patency not restored	1
Patency restored, no clinical improvement	none
Patency restored, good result	5
Patency restored, excellent result	7

a prolonged period of time and this is very essential in the successful surgical treatment. The results of surgery are summarized in Table v; the figures given refer to the 32 arteries operated upon. An abundant backflow of blood from the distal segment of the internal carotid at the time of surgery established patency of the anterior cerebral artery, middle cerebral artery or both. If such a backflow cannot be obtained, there is obviously no possibility of improvement.

It is readily apparent from this survey of results that a relatively small percentage of patients with *complete occlusion* are or can be helped by surgery. However, exploration is justified because no other form of treatment offers the patient any hope of improvement, and the risk is slight. On the other hand the patient with severe stenosis can almost always be dramatically improved. All of these patients with stenosis had serious symptoms which, before angiography, were clinically indistinguishable from many of those produced by complete occlusion.

Most of those patients with occlusion who were operated upon but were said to show no improvement actually improved to varying degrees. They followed the usual course of a stroke patient. In contradistinction, the patients said to have a restoration of function, were improved far beyond any spontaneous recovery that might be hoped for.

There were 5 deaths. In 3 it was not possible to establish patency of the carotid artery and they died three days, one week, and two weeks following operation. In 2 others the operation was highly successful but 1 died several weeks later of a coronary artery occlusion and 1 six weeks later of an intracerebral hemorrhage following a severe fright.

Of the 6 patients with complete occlusion in whom patency was established and no special improvement was experienced, 3 were found on postoperative arteriography to have occlusions of the middle cerebral artery and 1 had occlusion of the angular artery. (These patients should be diagnosed early and treated as acute surgical emergencies if complete occlusion is to be prevented.)

The visualization of the carotid siphon via collateral filling, when complete occlusion is present in the cervical internal carotid artery, is usually obtained in those cases where successful re-establishment of the circulation is possible. Figures 17, *A* and *B*, 18 and 19 illustrate 3 of the successful surgical cases. These "stroke" victims undoubtedly would have progressed to the usual hemiplegia, aphasia, or mental deterioration and possibly death. While this is only a promising beginning, the encouraging results obtained, along with the rapid improvement in vascular surgery, justify vigorous efforts at early diagnosis.

SUMMARY

This is a study of 1,535 patients who had had cerebral angiography including 626 consecutive examinations in which the cervical carotid artery, as well as the intracerebral vessels, were routinely visualized. Equipment alterations, permitting demonstration of the neck vessels on every cerebral angiogram, were initially made to better diagnose carotid occlusion. A study of the much broader problem of stenosis was an outgrowth. Much information on carotid insufficiency and cerebral ischemia was obtained—a condition which most commonly affects the brain and is the second most common cause of death.

Stenosis, of varying degree, was seen

three times more frequently than tumor, five times more frequently than aneurysm and fifteen times more frequently than arteriovenous anomaly. Carotid insufficiency is often clinically indistinguishable from tumor, intracerebral hemorrhage, cerebral embolus, or "idiopathic cerebral atrophy."

The process starts surprisingly early in middle life—it was observed coincidentally in patients as young as thirty-one years old and undoubtedly often exists for years before diagnosis. In the early or developing stage carotid insufficiency produces a variety of minimal symptoms: headache, mental disturbances, transient paresthesias, or speech disturbances that are usually ignored or casually dismissed. Yet, even at the present status of vascular surgery, some of these people can be successfully treated and should be so treated before a complete occlusion occurs.

This early surgical treatment is possible only if the disease process is suspected and the patient referred for angiography early. This should be done on patients of all types and all ages including those who have just suffered an acute cerebrovascular accident. This policy has proved safe.

Locations where stenosing plaques have been noted are those where complete occlusion most frequently occurs. Undoubtedly, stenosis leads to occlusion and treatment of the stenosing plaque prevents the later occlusion. Four types of stenosing disease have been observed, each with its own clinical and pathologic characteristics.

Correlation between carotid and cerebral vascular stenosis and atrophy was established.

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A METHOD FOR LOCALIZING THE PINEAL GLAND ON ANTEROPOSTERIOR PROJECTIONS

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NOT infrequently the radiologist is asked to evaluate roentgenograms of the skull for the position of the pineal gland. Unfortunately, because of the indications for such a request, the patient often is unable to cooperate or cannot be satisfactorily immobilized and some rotation is present on the roentgenogram. This paper describes a method in which a line determined by two mid-sagittal structures is used to localize the pineal gland in anteroposterior views of the skull.

The pineal gland may be localized in this view by measuring the widest transverse diameter of the skull, using either the inner or outer tables of the skull, and taking the mid-point of this distance as the normal pineal position. Fray[1] in 1936 showed that this method was relatively insensitive to rotation and that 15 degrees of rotation did not significantly alter the position of the pineal gland. This method has the disadvantage that one is not actually measuring the mid-sagittal plane of the brain and any asymmetry of the skull will introduce some error.

In 1940, Reinhold[5] described a method whereby a line drawn between the mastoid tips is bisected with a perpendicular line. If the pineal gland is not displaced, the perpendicular line will pass through the gland whether or not rotation is present. This method may be further simplified by the use of a compass in which the pineal gland is used as the center and arcs are drawn in the region of the mastoid tips. If the pineal gland is in normal position, these arcs will pass through both tips, even in the presence of rotation. However, again lateral skull structures are used and asymmetry will introduce some error.

Vastine and Kinney[6] have pointed out the two disadvantages of determining lateral displacement of the pineal gland in the anteroposterior projection; namely, (1) any rotation of the head makes accurate evaluation difficult, and (2) the gland is more difficult to visualize in this projection. Various techniques have been developed to assure a true anteroposterior projection. Naffziger[4] used a stethoscope with an attached pointer to aid in positioning the patient. Sosman employed a pelvimeter caliber with ear pieces in much the same manner. Since methods are available for localizing the pineal gland in the presence of rotation, such procedures are no longer necessary. Naffziger[4] pointed out that the second objection can be minimized by projecting the central ray caudally through the vertex so as to throw the frontal sinuses out of the projection of the pineal shadow.

PROCEDURE

A dried skull was designed with a lead pineal gland which was orientated both in normal and abnormal positions. Roentgenograms in the anteroposterior,* Chamberlain-Towne,† and posteroanterior views were then made in both the true projection and a projection with 10 degrees rotation. These were studied for mid-sagittal landmarks so situated anterior and posterior to the pineal gland that any rotation of the skull would shift one point to the left and the second to the right. A reference line connecting these two points would have the same position relative to the pineal gland in true and rotated views. The pseudopineal

* Anteroposterior view refers to an anteroposterior projection of the skull with the meatal-orbital line perpendicular to the film. The central ray passes through the pineal gland with a 20–25 degrees caudal tilt.

† Chamberlain-Towne view refers to an anteroposterior projection of the skull similar to the anteroposterior view, but the caudal tilt is increased 35 degrees.

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gland in various positions in the dried skull was localized by three observers, using the mid-point of the widest transverse diameter of the skull and the reference line described above.

These landmarks were applied to skull roentgenograms of patients with normally and abnormally placed pineal glands. In some cases roentgenograms in both true and rotated views were made and the position of the pineal gland was localized, using the method described by Fray as well as the reference lines described above and these results were compared.

RESULTS

In the anteroposterior and Chamberlain-Towne views of the dried skull, a line connecting the mid-point of the dorsum sellae and lambda passed through the normally placed pineal gland even in the presence of 10 degrees rotation. The relative position of the abnormally placed pineal gland to the line was similar in both the true and rotated projections. In the Chamberlain-Towne view, the posterior margin of the foramen magnum is visible, and it was found that a line connecting the opisthion and the bregma gave similar results. The intersection of these two lines was located within the normally placed pineal gland. In posteroanterior views, no anterior point could be identified which gave satisfactory results. These landmarks were all so far anterior that with rotation there was greater separation between the anterior landmark and the pineal gland than between the posterior landmark and the pineal gland. This resulted in an apparent pineal shift in a direction opposite to the rotation of the anterior landmark.

The localizations of the pseudopineal gland are shown in Table I. The localizations of the pineal gland in 16 patients are shown in Table II.

DISCUSSION

It is fortunate that these particular points gave satisfactory results because in the majority of skulls they can be identified. If difficulty is encountered in identifying the bregma or lambda, stereoscopic roentgenograms are of value in localizing these points. These points were more difficult to determine in the skulls of senile patients. Due to the projection in the Chamberlain-Towne view, there may be some difficulty in differentiating the bregma from the lambda. The fact that with rotation the bregma and lambda shift in opposite directions relative to one another and to the opisthion and the mid-point of the dorsum sellae respectively was of value in localization as were stereoscopic roentgenograms of the skull. These points and the above shift are illustrated in Figure 1.

One may maintain that the mid-point of the dorsum sellae is subject to the same error of asymmetry as the use of the widest transverse diameter of the skull; however, this structure is small enough that a slight asymmetry is detectable roentgeno-

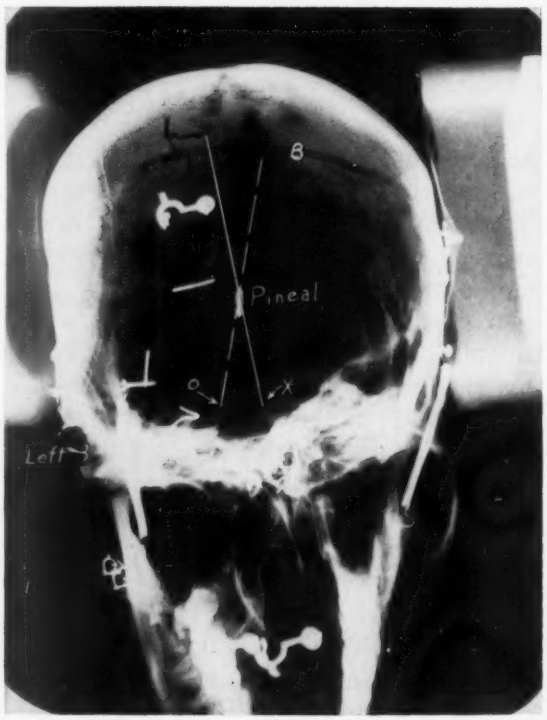

FIG. 1. A rotated anteroposterior roentgenogram of the dried skull to demonstrate the reference points (X = mid-point of dorsum sella, B = bregma, L = lambda, O = opisthion), the reference lines, and the manner in which the reference points change with rotation.

TABLE I

LOCALIZATION OF PSEUDOPINEAL GLAND IN DRIED SKULL

View	Method	Widest Transverse Diameter		Mid-Sagittal Landmarks (in mm.)
		Inside Tables (in mm.)	Outside Tables (in mm.)	
Anteroposterior[1]	True	1.2R (0.5–1.5)	0.5R	3.2R (3.0–3.5)
	Rotated (right)	1.3R (1.0–1.5)	1.0R (0.5–1.5)	3.7R (3.0–5.0)
Posteroanterior	True	3.0R (2.5–3.5)	2.2R (1.5–3.0)	2.8R (2.5–3.5)
	Rotated (right)	2.8R (0.5–4.0)	3.3R (2.5–4.0)	0.7L[2] (0.0–1.0)
Anteroposterior[1]	True	2.2L (1.5–3.0)	2.0L	0.8L (0.5–1.0)
	Rotated (right)[3]	3.8L (3.0–4.0)	3.7L (3.0–4.0)	0.2L (0.0–0.5)
Posteroanterior	True	1.5L	3.7L (3.0–4.0)	1.0L
	Rotated (right)	1.0L (0.5–2.0)	1.0L (0.5–2.0)	3.3L[2] (3.0–4.0)
Anteroposterior	True	1.2L (0.5–1.5)	2.2L (2.0–2.5)	0.3L (0.0–1.0)
	Rotated (right)	1.8L (1.0–3.0)	2.7L (2.5–3.0)	0.7L (0.5–1.0)
Anteroposterior	True	6.7R (6.0–7.5)	6.0R	6.2R (6.0–6.5)
	Rotated (left)	6.5R (6.0–7.0)	6.5R (6.0–7.0)	5.7R (5.0–6.0)
	Rotated (right)	6.3R (5.0–7.0)	6.7R (6.0–7.0)	6.7R (6.0–7.0)

Numbers in parenthesis are the range of localization by three observers and the number preceding the parentheses is the average of the three observations.

[1] Chamberlain-Towne view.

[2] Glabella used as the anterior point.

[3] Rotated 20°.

graphically. In some instances due to demineralization, the dorsum sellae is difficult to visualize, but the anterior clinoids are plainly seen. In such cases the midpoint of the distance between the anterior clinoids is a suitable substitute for the midpoint of the dorsum sellae if only slight rotation is present (Fig. 2). However, differences due to asymmetry are difficult to ascertain at these two points.

Fray[1] found a variation up to 2 mm. of the position of the pineal gland relative to the mid-point of the widest transverse diameter in 72 normal cases. For this reason he considers any shift less than 2 mm. to be within normal limits. He listed two theoretic reasons why such a range is necessary for a structure which should normally be in the mid-sagittal plane. These are: (1) If lateral structures are used, asymmetry will introduce error; and (2) the pineal gland may calcify eccentrically. If any rotation in the anteroposterior projection is present, a third reason is necessary because of the normal range of the position of the pineal gland in the anteroposterior diameter in the lateral view. This range will be a function of the normal variability of the pineal gland in the lateral view and the amount of rotation.

It is seen from Tables I and II that when using the mid-sagittal landmarks in the anteroposterior projection, the maximum shift with rotation was 1 mm. In the posteroanterior projections using mid-sagittal landmarks, the differences with rotation were 3.5, 2.3, and 1.5 mm. The explanation of this is given under RESULTS.

The position of the pineal gland in true and rotated anteroposterior and posteroanterior projections when localized by use of the mid-point of the widest transverse diameter differed by less than 2 mm. except in those cases in which the rotation exceeded the 15 degrees limit suggested by Fray and in Case 8, Table II. Here, in addi-

TABLE II

COMPARISON OF PINEAL GLAND LOCALIZATION USING THE MID-POINT OF WIDEST DIAMETER AND MID-SAGITTAL LANDMARKS IN TRUE AND ROTATED ANTEROPOSTERIOR VIEWS

Case No.	View	Position of Pineal Gland	
		Mid-Point of Transverse Diameter (in mm.)	Mid-Sagittal Landmarks (in mm.)
1	Anteroposterior, no rotation	2.0L	2.0L
	Anteroposterior, 15° rotation to right	1.5L	2.0L
	Anteroposterior, 20° rotation to right	4.0L	2.0L
	Anteroposterior, 20° rotation to left	2.5R	3.0L
	Posteroanterior, no rotation	2.0L	1.5L
	Posteroanterior, 15° rotation to left	1.0L	0.0
2	Anteroposterior, no rotation	10.0L	10.0L
	Anteroposterior, marked rotation	( )[1]	9.0L
3	Anteroposterior, no rotation	0.5L	0.0
	Anteroposterior, marked rotation	0.5L	0.0
4	Anteroposterior, no rotation	1.5R	2.0R
	Anteroposterior, marked rotation to left	2.0R	1.0R
	Anteroposterior, marked rotation to right	0.0	2.0R
5	Anteroposterior, no rotation	1.5R	1.0R
	Anteroposterior, moderate rotation to left	3.5R	1.0R
	Anteroposterior, moderate rotation to right	0.0	0.0
6	Anteroposterior, no rotation	7.0R	6.0R
	Anteroposterior, marked rotation to right	4.0R	6.0R
	Anteroposterior, marked rotation to left	9.0R	7.0R
7	Anteroposterior, no rotation	0.0	0.0
	Anteroposterior, moderate rotation to right	2.0L	0.0
	Anteroposterior, moderate rotation to left	0.0	1.0R
8	Anteroposterior, no rotation	0.0	0.0
	Anteroposterior, marked rotation to right	6.0L[2]	0.0
	Anteroposterior, marked rotation to left	3.0R[2]	0.0
9	Anteroposterior, slight rotation	1.5R	1.5R
10	Anteroposterior, no rotation	0.0	0.0
11	Anteroposterior, slight rotation	0.0	0.0
12	Anteroposterior, slight rotation	0.0	0.0
13	Anteroposterior, slight rotation	5.0R	6.0R
14	Anteroposterior, slight rotation	0.5R	1.5R
15	Anteroposterior, slight rotation	2.0L	2.0L
16	Anteroposterior, no rotation	1.0L	0.0

[1] Unable to measure because one side of skull was off the film.
[2] Apparently some asymmetry with slight flattening of left side.

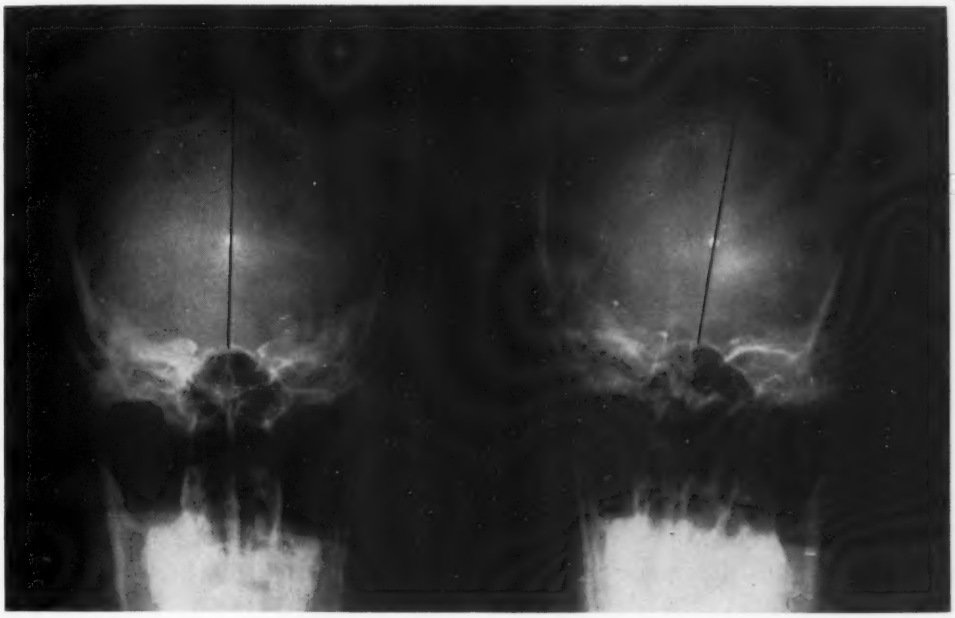

Fig. 2. Skull roentgenograms demonstrating the use of the mid-point of the distance between the anterior clinoids in place of the mid-point of the dorsum sellae. The appropriate anatomic structures were retouched so they would show on roentgenograms.

tion to the rotation being marked, there was some asymmetry of the skull with the left side being somewhat flattened.

It was noted when using the mid-point of the widest transverse diameter in anteroposterior and Chamberlain-Towne views, that the rotation produced an apparent shift of the pineal gland in the opposite direction to the rotation of the anterior aspect of the skull. This was true where the rotation was slight and the differences in localization in the true and rotated views were slight (1.0–1.5 mm.). It appears that the axis of rotation, the curvature of the parietal bones, and the position of the pineal gland are such that rotation produces an apparent, but slight, shift of the pineal gland relative to the projection of the lateral skull margins on the roentgenogram opposite to the direction of rotation. This was not true when mid-sagittal landmarks were used.

In Table 1 on all localizations excepting those with a marked shift, the position of the pineal gland as determined by the widest transverse diameter was approximately 1 to 2 mm. to the left of the position determined by the use of mid-sagittal landmarks. The fact that this difference was always to the same side strongly suggests that there is a factor other than slight inaccuracies in measurements, and a possible explanation would be a slight asymmetry of the skull with the left side being smaller. When the transverse section of the skull was checked, this was shown to be true.

It is obvious that if the pineal gland is not at the center of rotation, an apparent shift of this gland will be projected onto rotated anteroposterior roentgenograms. The extent of this shift will depend upon the degree of rotation (θ) and the distance of the pineal from the axis of rotation (d). The shift from the mid-line will be $d \sin \theta$.

It is not necessary, however, that the pineal gland be localized in the axis of rotation for the use of the mid-point of the widest transverse diameter or of mid-sagittal landmarks to be insensitive to rotation. In the former the radius of curvature of the parietal bone lateral to the pineal gland may be such that the change in the projection of the skull table would compensate for any change of the position of the pineal gland due to rotation. In the latter method the anterior and posterior landmarks were

so chosen that rotation produced equal but opposite shifts of the points from the pineal gland. Nevertheless, a change from a normal position of the pineal gland along the anteroposterior diameter will affect its position in a rotated anteroposterior view, and the extent of the normal range in the lateral view will define a limit of variability in rotated anteroposterior views which will increase as the degree of rotation increases.

Lilja[3] in 1934 localized normal pineal glands with respect to 11 measurements in the lateral skull views of 769 patients. The diameter which quite closely approximates the anteroposterior diameter of the skull which is traversed by the central ray in anteroposterior skull projections was 18.68 cm., with a standard deviation of 1.12 cm. The possibility of this diameter in any patient exceeding 21.60 cm. (18.6 cm. $+2.5\times1.12$ cm.) is less than 5 out of 1,000. In describing his proportional method for localization of the pineal gland in the lateral skull view, Fray[2] gives a range of 5 per cent of the anteroposterior diameter. The range in centimeters for the largest skulls is 0.05×21.6 cm. or 1.08 cm. This is in agreement with the range of 1 cm. on Vastine and Kinney's charts.[6]

Using a normal range of 1 cm., we can calculate the maximum degree of rotation which can be tolerated in the anteroposterior projection permitting a normal range in this projection of 0.2 cm. This is done for two situations since we do not know the position of the axis of rotation. If the axis of rotation passes through the mid-point of the normal range of the position of the pineal gland, d equals one half of the normal range and the change with rotation is a minimum. However, if the axis of rotation lies outside the normal range of the position of the pineal gland in the anteroposterior diameter, then d equals 1 cm. and the shift is maximum. In the former case 0.2 cm. $=0.50$ cm. Sin θ or $\theta=23.6°$; and in the latter, 0.2 cm. $=1.0$ cm. Sin θ or $\theta=11.4°$. Hence, moderate degrees of rotation will not produce intolerable apparent shifts of the pineal gland due to the normal variability of the position of the gland on lateral projections. It is possible that the product of an actual anterior or posterior shift of the pineal gland and the sine of the degrees of rotation of an anteroposterior skull roentgenogram would compensate for a slight pathological shift to the right or left. However, this is improbable and in any case could be checked by evaluating lateral skull films or anteroposterior views rotated in a direction opposite and approximately equal to the rotation on the films in question.

There are occasions when due to trauma or surgery, or because of obvious asymmetry of the parietal region of the skull, midsagittal landmarks must be used to evaluate the pineal gland. Frequently, such patients cannot be positioned properly or cannot be properly immobilized. In these instances, the method described here is of value (Fig. 3).

The anteroposterior roentgenograms described in this paper and made routinely at this institution were made as suggested by Naffziger[4] in that the caudal tilt throws the frontal sinuses out of the projection of the pineal gland. Nevertheless, not infrequently there is some question as to whether or not a density is the pineal gland, or faintly calcified pineal glands are obscured by the occipital ridge. Usually stereoscopic views are of value, particularly in differentiating two densities; however, in case that stereoscopic equipment is not available or if the patient cannot be properly immobilized for stereoscopic views, another approach is possible. Since the pineal gland can be accurately localized in the presence of a moderate degree of rotation, anteroposterior roentgenograms with approximately 10 degrees of rotation to the right and left can be taken and the position of the suspected density evaluated. Unless the density is the pineal gland or a calcified density in very close proximity to the pineal gland, there is a significant change in position in the

Fig. 3. An anteroposterior roentgenogram of a postoperative skull. The localization of the pineal gland was the same using the mid-point of the widest transverse diameter and the mid-sagittal reference line. However, the radiologist who reported this case was accustomed to using the mid-point of the widest transverse diameter and suspected that the pineal shift here might have been caused by the slight elevation of the bone flap. The anatomic points of interest were retouched so these would show on the roentgenogram.

⟹→

two rotated views (Fig. 4). Figure 5 demonstrates a case in which a faint indefinite density in the true anteroposterior projection is better visualized on anteroposterior roentgenograms rotated to the right and left. The reference lines intersect within this density, showing that it lies in the position of the normal pineal gland.

CONCLUSIONS

1. On both anteroposterior and Chamberlain-Towne roentgenograms of the skull a line connecting the mid-point of the dorsum sellae to the lambda and a line connecting the opisthion to the bregma passes through the normally placed pineal gland whether or not rotation is present. If the pineal gland is abnormally placed, its posi-

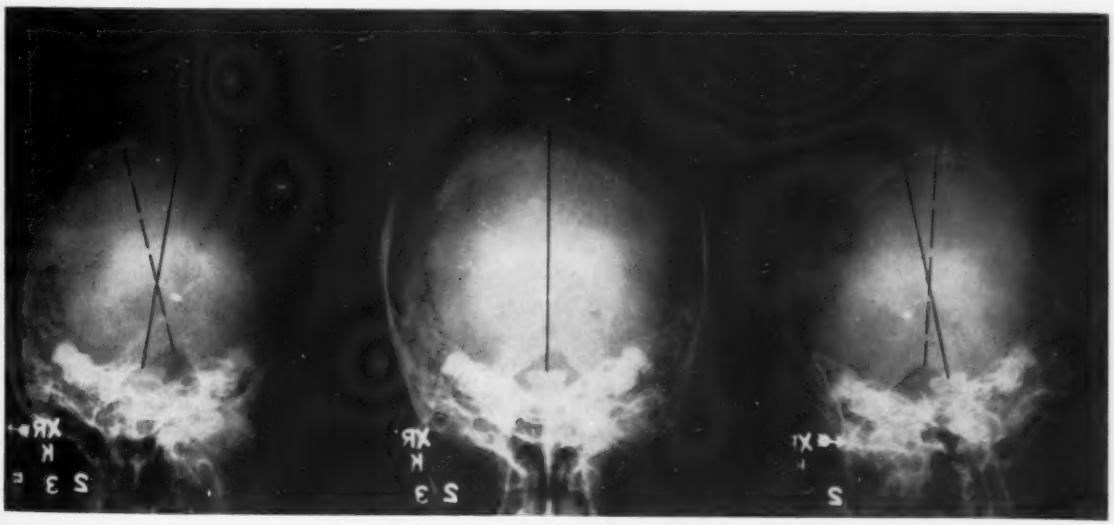

Fig. 4. These roentgenograms demonstrate a case in which a density which was thought to represent the pineal gland was shown to rotate away from the reference lines and to lie posterior to the normal position of the pineal gland. In both rotated views an indistinct area of calcification was noted at the intersection of the two lines and in retrospect could be suspected in the true anteroposterior view as lying in the mid-sagittal plane superior to the more prominent density. The necessary anatomic structures were retouched so they would show on the roentgenograms.

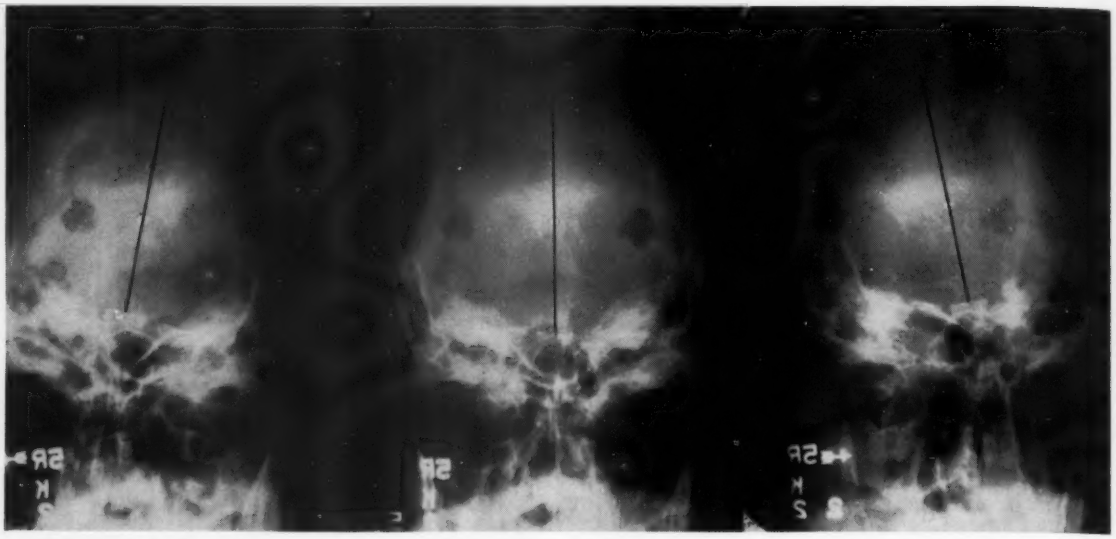

FIG. 5. Roentgenograms of a skull in which the faint calcification in the position of the normal pineal gland is visualized in the rotated views with more certainty than in the true anteroposterior view. The appropriate anatomic landmarks were retouched so that they would show on roentgenograms.

tion relative to the reference lines is unchanged with rotation, provided the position in the lateral view is within normal limits.

2. On posteroanterior roentgenograms, no anterior landmark could be found which fulfills the necessary criteria. These all shifted farther with respect to the pineal gland than did the posterior landmark, giving the appearance of a shift of the pineal gland.

3. Due to a normal variation in the position of the pineal gland in the anteroposterior diameter of the skull, a normal range on rotated anteroposterior skull roentgenograms must be defined which will increase with the degree of rotation. When the extent of rotation is slight, this range is only 1 or 2 mm.; hence, small shifts of the pineal gland on rotated anteroposterior skull roentgenograms must be evaluated.

4. Since the pineal gland can be adequately localized on rotated anteroposterior roentgenograms of the skull, such roentgenograms can be used to advantage to better visualize faintly and indistinctly calcified pineal glands.

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A NEW METHOD FOR LOCALIZING THE CALCIFIED PINEAL GLAND ON THE LATERAL SKULL ROENTGENOGRAM*

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THE change in position of the calcified pineal gland as an important sign in localization of intracranial lesions was first pointed out by Naffziger in 1925.[4] Two years later Vastine and Kinney[5] described a method of localizing the calcified pineal gland on the lateral roentgenogram of the skull in which four points of reference on the inner table were utilized. The points were: frontal, occipital, vertex and base. In 1934 Lilja[3] made a series of measurements utilizing many points of the internal table for evaluation of pineal gland localization. Fray[1] in 1937 described a method similar to that of Vastine and Kinney with the same points of reference; however, he utilized an elastic band marked off to delineate the limits of the normal pineal gland. This allowed an increase in the area of normality in the larger skull. He described this as a "proportional" method. In 1955 Geffen[2] described a "ruler-graph" for localization of the pineal gland on the lateral roentgenogram. This is based on the Vastine and Kinney method with certain modifications.

This is a report on another method which utilizes points of reference other than those of the internal table.

MATERIAL

True lateral skull roentgenograms were done on 121 Duke Hospital patients. These patients were questioned as to neurologic complaints. All had been brought into the hospital and were being treated for conditions not indicative of central nervous system disease. Only those patients over thirty years of age presenting calcified pineal glands were included in this study (Table I).

A second series of skull roentgenograms of 28 patients with known intracranial lesions and calcified pineal glands was also examined (Table II.)

TECHNIQUE

A line was extended from a point located at the middle of the base of the nasal bone (nasofrontal articulation) to a point located mid-way between the anterior and posterior clinoids. A second line was then extended from this interclinoid point to the middle of the pineal calcification. The habenula was included as a portion of the pineal calcification since the two are so frequently inseparable roentgenographically. A measurement of the superior angle was carried out with an angle measuring device. The distance between the interclinoid point and the midpoint of the pineal calcification was measured with a standard centimeter ruler. The points of reference are illustrated in Figure 1.

The measurements thus obtained were compared with those obtained by use of the Geffen ruler-graph* and the pineal calculator† as used at the Neurological Institute, New York City.

RESULTS

In the group of 171 clinically normal patients over the age of thirty years, a calcified pineal gland was detectable in 121, or 71.3 per cent. The nasopineal angle had a range in this group of 135° to 161° with an average of 148°. From these data a range of normal with a 95 per cent confidence limit for the nasopineal was found to be 138.5 to 157.5 degrees.

The sella turcica to pineal gland distance

* Obtained from Picker X-ray Corporation, 25 South Broadway, White Plains, New York.
† Obtained from Ansco, Binghamton, New York.

* From the Department of Radiology, Duke University Medical Center, Durham, North Carolina.

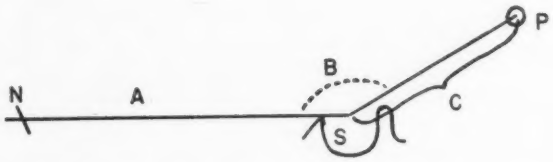

Fig. 1. Diagram showing the distance between the interclinoid point and the midpoint of the pineal calcification.
N. Base of nasal bone.
A. Nasal to sella turcica line—passing through midpoint of "N" to midpoint between anterior and posterior clinoid and on same level as tips.
B. Nasopineal angle; normal range (95 per cent confidence) 138.5 to 157.5 degrees.
S. Sella turcica.
C. Sella turcica to pineal gland line; normal distance (95 per cent confidence) 3.9 to 5.3 cm.
P. Pineal gland.

had an over-all range of 3.4 cm. to 5.4 cm. with an average of 4.6 cm. The range of normal with a 95 per cent confidence limit for the sella turcica to pineal gland distance is 3.9 to 5.3 cm.

The series of patients with proved space occupying intracranial lesions showed that only 10 had pineal glands within normal range by all three methods. A further analysis of this study is shown in Table II.

Table I

Comparison of 121 clinically normal patients

Method of Localization	Within Normal Range	Outside of Normal Range
New York City Neurological Institute	100	21
Geffen Ruler-graph	101	20
Nasopineal*	108	13
All Three Methods	83	1
Nasopineal and New York City Neurological Institute Method	90	2
Nasopineal and Geffen Ruler-graph	90	2
New York City Neurological Institute Method and Geffen Ruler-graph	91	11

* 95 per cent confidence limit applied.

Table II

Comparison of 28 patients with expanding intracranial lesions

Method of Localization	Within Normal Range	Outside of Normal Range
New York City Neurological Institute	15	13
Geffen Ruler-graph	19	9
Nasopineal	17	11
All Three Methods	10	5
Nasopineal and New York City Neurological Institute Method	10	6
Nasopineal and Geffen Ruler-graph	11	5
New York City Neurological Institute Method and Geffen Ruler-graph	14	7

Discussion

This method of localizing the pineal gland on the lateral roentgenogram utilizes points of reference which appear to be more definite and more fixed than in the methods which have been previously described. This fact might offer an advantage in that there is less likely to be any subjective element present in the interpretation.

This procedure may be carried out by marking three points on the film. With this phase of the operation, there is no room for subjective influence. If then the appropriate lines are drawn, and the angle and distance measured, this also becomes an objective procedure.

The ease with which this method may be carried out offers a very definite advantage.

Using the above findings, a localizer may

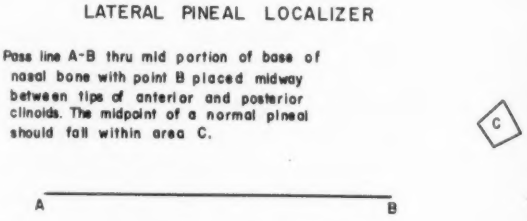
LATERAL PINEAL LOCALIZER
Pass line A-B thru mid portion of base of nasal bone with point B placed midway between tips of anterior and posterior clinoids. The midpoint of a normal pineal should fall within area C.
C
A
B

Fig. 2. Lateral pineal localizer.

be designed which when superimposed on the lateral skull roentgenogram shows immediately whether there is displacement of the pineal gland and, if so, how much and in what direction (Fig. 2).

SUMMARY

A new method of localizing the calcified pineal gland on the lateral skull roentgenogram is described. This utilizes reference points on the base of the nasal bone, the sella turcica and the pineal gland.

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THE ROENTGENOLOGIC ASPECTS OF TYMPANOPLASTY*

AN OTOLOGIST'S VIEWPOINT

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THE concept of otologic surgery has been revolutionized within the lifetime of the present medical generation. Chemotherapy and antibiotics have dramatically decreased the number of mastoidectomies necessary for the treatment of acute mastoiditis and petrositis. The introduction of practical fenestration for the improvement of hearing was the first great stride in the surgical treatment of deafness. Transtympanic stapedial footplate surgery has further broadened the scope of the operative treatment of otosclerosis.

The diminution in the incidence of acute mastoiditis proportionately decreased the incidence of requests for roentgenologic examinations of the temporal bone. The increase in surgical procedures for the relief of the hearing loss of otosclerosis, however, was not reflected in an increased number of roentgenologic examinations, since otosclerosis cannot be demonstrated roentgenologically. Preoperative roentgenograms taken for medicolegal purposes only, before fenestration surgery, have led, if anything, to roentgenograms of poor quality and have promoted careless technique and haphazard interpretation.

The recent introduction of the concept of tympanic cavity reconstruction for the restoration of serviceable hearing through the procedures of myringoplasty and tympanoplasty, rather than the purely destructive concept of radical mastoidectomy, has afforded a new opportunity for the radiologist to provide important information before temporal bone exploration is undertaken.

The success of tympanic cavity reconstruction depends principally upon: (1) eradication of infection; (2) normal eustachian tube function; and (3) maintenance of an intact, viable skin graft closing the new tympanic cavity.

The surgeon is no longer primarily interested in the anatomy of the mastoid process and pathologic changes within its pneumatic system.[4,6] Except in revisions, statements such as those referring to the situation, width, breadth, etc., of the lateral sinus are of absolutely minor importance, because every surgeon past the beginner's stage has learned to find the lateral sinus without any difficulty during the operation and to avoid injuring it.[3] The classification of mastoids into pneumatic, nonpneumatic, and mixed types, while affording some knowledge of the general structure of the temporal bone, has never been of any real value to the otologist, and it must be admitted that little distinction can be made between the noncellular types on a roentgenologic basis.[5] A more useful classification has been suggested by Diamant.[2]

The surgeon now requires accurate information concerning the extent and activity of disease in the attic and aditus (Fig. 1 and 2). The less surgical exploration necessary, the better the blood supply in the site of the skin graft, and thus, the better chance of the maintenance of a viable graft.

Likewise, if exploration of the hypotympanum and eustachian tube orifice can be avoided, the graft has a better chance of taking. Although the otologist can, by inflation, evaluate the patency of the tube to the passage of air from the nasopharynx to the middle ear, he cannot tell whether or not the tube will clear the tympanic cavity of secretions. Patency of the tube to infla-

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Fig. 1. Owen's position. Malleus and incus intact. Arrows indicate well-defined area of bone destruction in the epitympanic space. A typical "attic" cholesteotoma. (Reproduced by permission from Dr. George E. Shambaugh, Jr., and the W. B. Saunders Company.)

Fig. 2. Mayer's position. Malleus and incus appear intact. Arrows indicate an obvious area of bone destruction in the epitympanic space which extends into the aditus. Another typical "attic" cholesteotoma. (Reproduced by permission from Dr. George E. Shambaugh, Jr., and the W. B. Saunders Company.)

tion and the ability of the tube to clear secretions from the middle ear are not synonymous.

The continuity of the ossicular chain can be determined rather accurately by various audiometric studies including the use of the acoustic probe. In cases of discontinuity of the ossicular chain, however, the condition and position of the malleus and incus can be determined roentgenologically (Fig. 3 and 4). At the present time, the incudostapedial joint and stapes cannot be satisfactorily identified.

Such conventional positions as the Chamberlain-Towne[14] and base view of the skull have little value in the examination of chronic cases because, although the tympanic cavity and antrum are visible, the relatively great mastoid-to-cassette distance produces loss of detail and clarity of projection; and in the Law position,[8] the attic-aditus-antral area is obscured entirely (Fig. 5 and 6). Laminagrams, while holding promise of great value in the future, have as yet revealed no more information than a good stereoscopic examination taken in properly chosen positions.

Since it is impossible to demonstrate all the desired anatomic features of the temporal bone sufficiently well by means of any one projection, multiple exposures, each designed to portray some particular feature of the temporal bone, are essential.

Mayer[9] in 1926 recommended a mastoid series consisting of stereoscopic roentgenograms taken in Schüller's, Stenvers', and Mayer's projections. Schüller's position,[9]

Fig. 3. Owen's position. There is a well-defined area of bone destruction in the epitympanic space extending into the aditus. The arrows indicate erosion of the long process of the malleus and of the incus.

Fig. 4. Owen's position. A postoperative modified radical mastoidectomy cavity. The "bridge" is down. The arrow indicates the malleus. The incus appears to be missing. At surgery it was found to have been displaced into the tympanic cavity in a previous operation.

taken laterally from a cephalocaudad angle of 25 to 30 degrees, reveals the pneumatic structure of the mastoid process, as well as the sinus and dural plates (Fig. 7).

Stenvers' position[13], taken from a caudocephalad angle of 12° with a 45° rotation of the head to bring the petrosa parallel to the film, projects the antrum to the best advantage (Fig. 8). The labyrinth, dural plate, the area of the tympanic cavity, and the cellular structure of the mastoid process are also visible. Unfortunately, there is no possible plane of projection by which one can bring the petrous pyramid directlv onto the film, or avoid confusion by the projection of other osseous anatomic parts upon it. The visualization of the petrosa through the temporal fossa and the occipital bone, as in Stenvers' position, makes this the most desirable view for the examination of the cochlea, internal auditory canal, and the cellular structure of the petrous pyramid.

For the examination of the temporal bone in chronic otitis media and mastoiditis, the Mayer position[9] gives information unobtainable in any other view except for the Owen modification. Only in these projections can the attic and aditus be satisfactorily visualized. In Mayer's position the malleus and incus, if present, should be seen in the upper tympanic and epitympanic cavities, and the antrum is visible above the arcuate eminence. The external auditory canal, the sinus and dural plates, and the cellular structure of the mastoid process are also visible (Fig. 9).

Taken from a cephalocaudad angle of 45°, with from 30 to 45 degree rotation of the face away from the film, the tympanic

Fig. 5. Schüller's position. A three year old child with a chronic draining ear. This roentgenogram shows only a "sclerotic" mastoid.

Fig. 6. Owen's position. By rotating the head 30° away from the film, a definite area of bone destruction is visible in the epitympanic space. A large aural polyp was originating from this area.

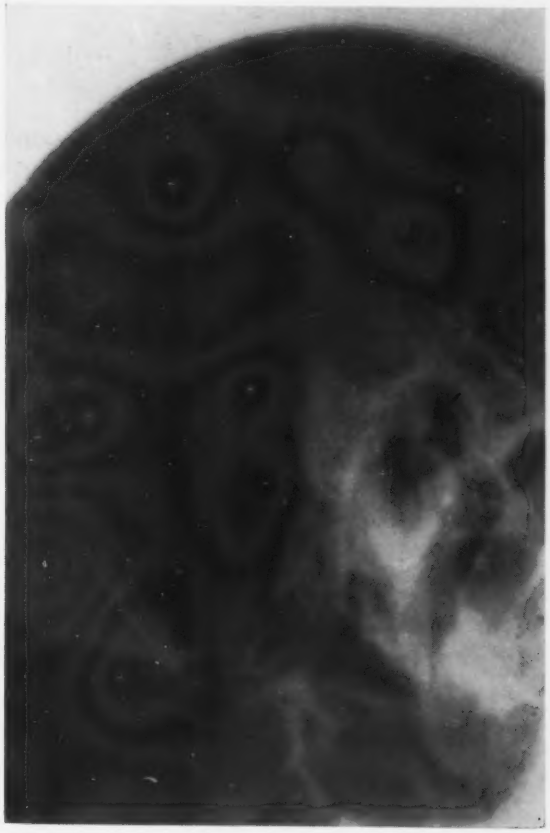

Fig. 7. Schüller's position, normal. The arrow indicates the head of the malleus visible in the epitympanic space above the anterior margin of the petrosa.

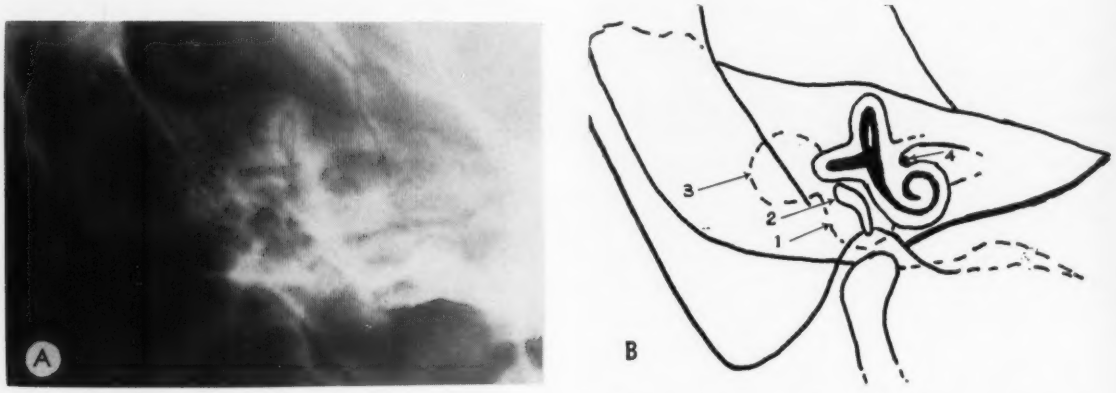

Fig. 8. Stenvers' position. (*A*) Normal roentgenogram. (*B*) Line drawing of *A*: 1. Area of tympanic cavity; 2. combined shadow of the malleus and incus; 3. area of the antrum; 4. hiatus for the facial canal. (Reproduced by permission from Dr. George E. Shambaugh, Jr., and the W. B. Saunders Company.)

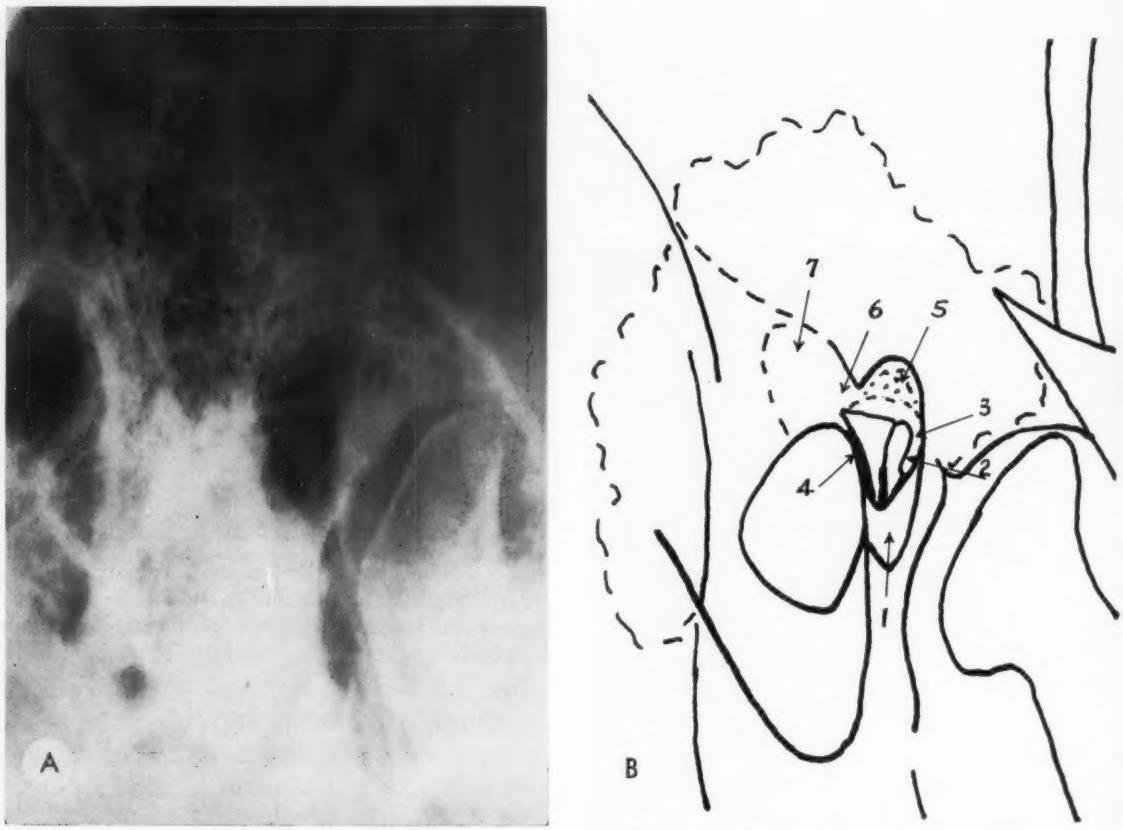

Fig. 9. Mayer's position. (*A*) Normal roentgenogram. (*B*) Line drawing of *A*: 1. External auditory canal; 2. tympanic cavity; 3. malleus; 4. incus; 5. epitympanic cavity with its normal osseous pattern; 6. area of the aditus; 7. area of the antrum. (Reproduced by permission from Dr. George E. Shambaugh, Jr., and the W. B. Saunders Company.)

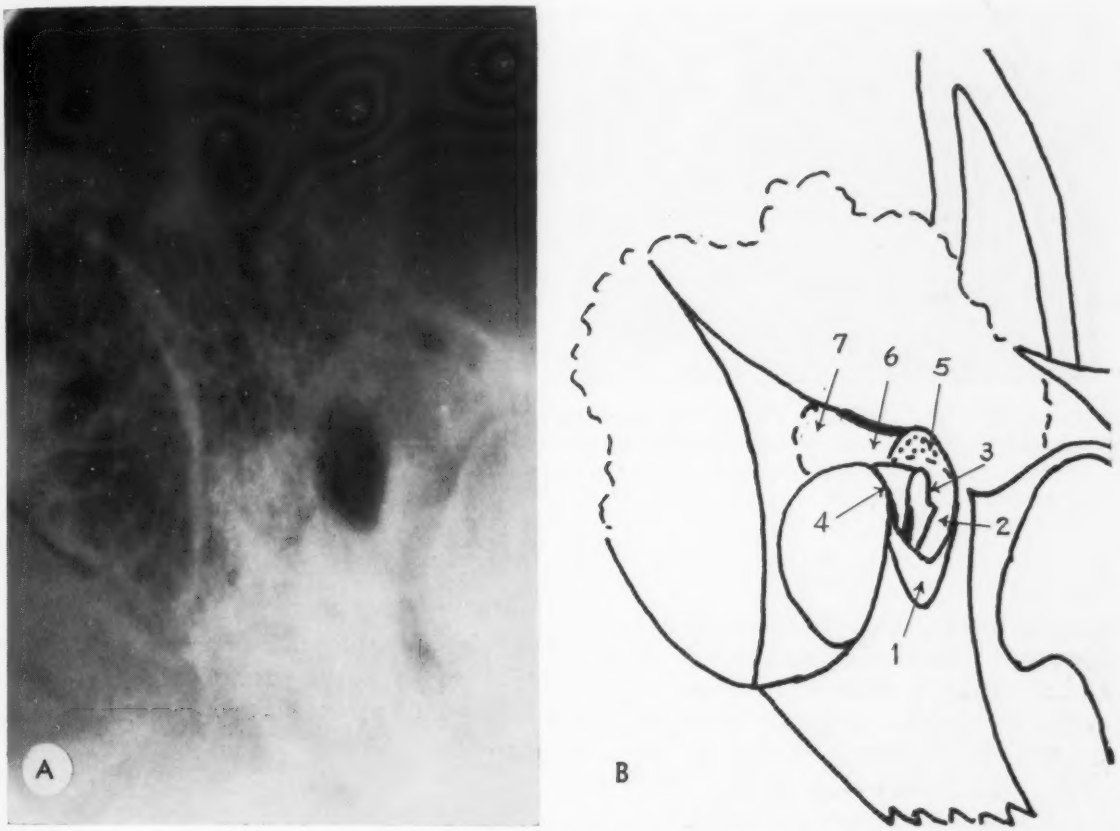

Fig. 10. Owen's position. (*A*) Normal roentgenogram. (*B*) Line drawing of *A*: 1. External auditory canal; 2. tympanic cavity; 3. malleus; 4. incus; 5. epitympanic space with its normal osseous pattern; 6. area o aditus; 7. area of the antrum. (Reproduced by permission from Dr. George E. Shambaugh, Jr., and the W. B. Saunders Company.)

cavity, attic and aditus are freed from the dense osseous shadow of the labyrinth. For the best detail, a two-inch cone is desirable. The closest possible mastoid-to-cassette apposition must be maintained. The mastoid can be placed firmly on the cassette only if a cassette holder is used which can be positioned above the patient's shoulder.[11]

The Owen position,[12] taken from a cephalocaudad angle of 30° with the same rotation as described above, amplifies the Mayer position by decreasing the distortions created by its 45° angulation. This position is preferred by the otologist because the attic-aditus-antral area has the same anatomic relationship as it does at the time of the surgery (Fig. 10).

In the usual case of chronic mastoiditis and otitis media, all other projections may be omitted without sacrifice, if correctly positioned stereoscopic projections are secured in Stenvers', Mayer's and Schüller's positions.[7]

The ability of the eustachian tube to clear the tympanic cavity can be examined roentgenologically, both by visualizing the tube filled with contrast material (Fig. 11 and 12)[10] and by determining the emptying time of the middle ear after a radiopaque fluid has been instilled into it.[1]

The patient should be seated in the erect position before a head unit. The middle ear can be filled with a contrast medium, such as pantopaque or hypaque, by means of a short bevel 25-gauge needle, either through the perforation present, or by injecting through the intact drum. No anesthesia is necessary. If the drum is perforated the external canal should be closed by means of a rubber or a paraffin ear plug

Fig. 11. Stenvers' position. The arrows indicate pantopaque in the hypotympanum and eustachian tube after instillation through a perforation in the tympanic membrane.

after the radiopaque material has been instilled.

A roentgenogram is taken immediately in Stenvers' postion. If any delay is allowed and the tube is functioning properly, the tympanic cavity may clear before the film is exposed. A normally functioning eustachian tube should clear almost all of the contrast material from the middle ear before the clearance roentgenogram is taken at the end of ten minutes. If the middle ear does not clear, exploration of the hypotympanum and tubal orifice becomes mandatory. When, however, the tympanic cavity clears readily, the surgeon may feel sure that the hypotympanum and eustachian tube are free from obstructive disease (Fig. 13).

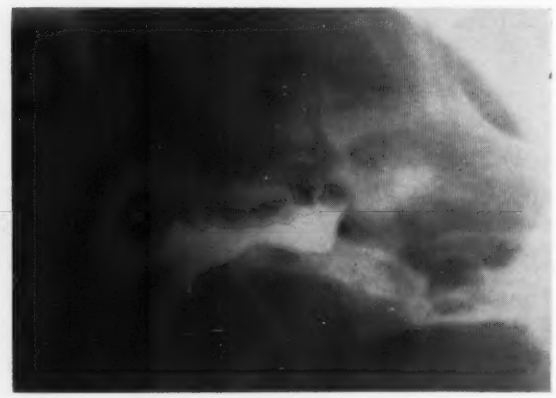

Fig. 12. Stenvers' position. The arrow indicates obstruction at the tympanic end of the eustachian tube in spite of good filling of the tympanic cavity. (Reproduced by permission from the American Academy of Ophthalmology and Otolaryngology Transactions.)

Fig. 13. Base view of the skull. This patient has an intact tympanic membrane and a normally functioning eustachian tube. The double arrows indicate the tympanic cavity filled with contrast medium. The single arrows indicate the entire eustachian tube filled with opaque material from the hypotympanum to the nasopharynx.

Conclusions

By the use of properly chosen and properly positioned temporal bone roentgenograms, the radiologist is in a position to give the otologist extremely useful information about the extent of disease in the middle ear, attic, and aditus, as well as the condition of the malleus and incus.

Tympanic cavity clearance studies give information concerning the ability of the eustachian tube to clear secretions from the middle ear, which, at this time, can be determined in no other way.

The otologist must have the courtesy to furnish the radiologist with the clinical history and physical findings prior to the roentgenologic examination, as well as the reports of the operative and pathologic findings if surgery is undertaken. In no other way can the radiologist determine the accuracy of his reports. On the other hand, the roentgenologist should attempt to keep abreast of the surgical developments in otology, and give the surgeon films depicting the diseased area, and information which

will be useful in the preoperative evaluation of the patient.

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OSTEOBLASTIC METASTASES TO THE FLOOR OF THE SKULL SIMULATING MENINGIOMA EN PLAQUE*

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APPROXIMATELY ten years ago the authors saw the roentgenograms of 2 patients with osteoblastic skull metastases simulating the hyperostosis associated with meningioma *en plaque*. The primary site of the tumor was the breast in one instance and the prostatic gland in the other. In this regard, in 1953, Schaerer and Whitney[3] reported a case of osteoblastic skull metastases from a primary prostatic carcinoma which they had mistaken for a meningioma and cited one additional case from the literature.[1] Because this entity is not widely known, it is being reported at this time.

REPORT OF CASES

CASE I. H.D., a forty-seven year old white female, was admitted on August 4, 1947, four years after a left radical mastectomy and bilateral oophorectomy for a breast carcinoma. Eleven months before admission she began to have vague discomfort in the left side of her throat and upper face. This disappeared after a few months but she soon noted recurring, bilateral, dull, supraorbital headaches.

The family history was of interest in that her sister died of gastric carcinoma and her father died of carcinoma of the rectum.

Physical examination was negative except for slight bilateral fundal pallor with blurring of both temporal margins and questionable slight weakness of the right upper extremity. Roentgenograms of the skull showed marked sclerosis of the floor of the left middle fossa (Fig. 1, 2 and 3). The clinical and roentgenographic impression was meningioma of the left middle fossa.

A left temporal craniotomy was performed on August 6, 1947. At operation, the bone of the floor of the middle fossa appeared to be grossly involved by tumor but no extraosseous tumor mass was found. Biopsy of the bone showed diffuse metastatic carcinoma.

CASE II. C.J.U., a seventy-two year old male, was admitted on November 6, 1944, four years after a two stage prostatectomy for "benign prostatic hypertrophy" with pain in the left face and forehead of ten months' duration. He also complained of failing vision and progressive left exophthalmos.

Physical examination disclosed some impairment of sensation and pain along the third division of the left trigeminal nerve and some hypesthesia of the left arm and leg. Visual acuity corrected was O.D. 13/15+3 and O.S. 13/25 −2. Roentgenograms of the skull showed extensive sclerosis of the floor of the anterior and middle fossae extending into the left zygoma (Fig. 4 and 5). The clinical impression was left supraorbital meningioma.

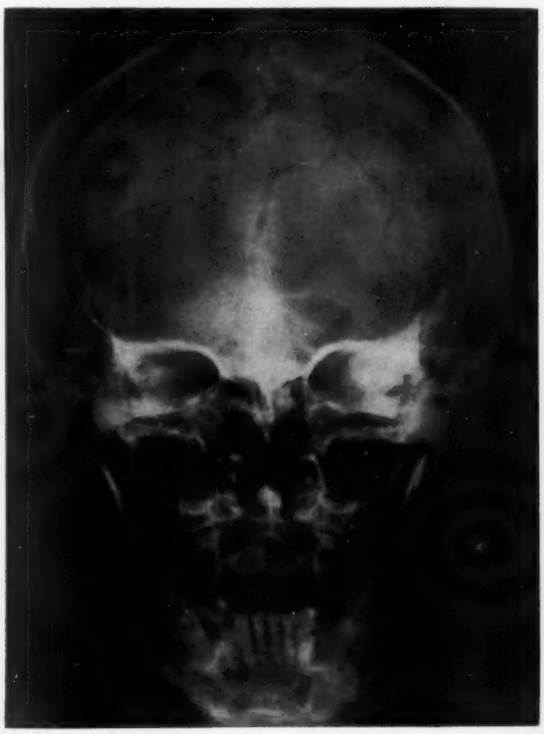

FIG. 1. Case I. Posteroanterior roentgenogram of the skull showing sclerosis of the left greater sphenoidal wing.

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Fig. 2. Case I. Roentgenogram in Waters' view demonstrating involvement of the left zygomatic bone.

Fig. 4. Case II. Roentgenogram in Waters' view showing sclerosis of the left greater sphenoidal wing and zygoma.

A craniotomy was performed on November 11, 1944. The bone in the left temporal region was considerably thickened. In the left Sylvian fissure, apparently arising from the pterional region was a tumor the size of a small apple. A partial removal of the tumor was accomplished but the patient expired on the following day. At autopsy, the small residual prostate was quite firm. Microscopic examination revealed adenocarcinoma of the prostate with metastases to the left anterior and middle fossae, orbit and zygoma.

COMMENT

The syndrome of unilateral gradual loss of visual acuity associated with nonpulsat-

Fig. 3. Case I. Left lateral roentgenogram illustrating the marked increased density of the middle fossa.

Fig. 5. Case II. Left lateral roentgenogram demonstrating sclerosis of the middle fossa.

ing exophthalmos and hyperostosis of the floor of the skull has long been associated with meningioma *en plaque*. In Cushing and Eisenhardt's[2] classic monograph, meningioma *en plaque* is reported as occurring more commonly in women in the fourth decade of life. A more rapid onset of exophthalmos and decreased visual acuity, particularly in older patients and especially in older males, should raise the suspicion of metastatic carcinoma. The latter diagnosis should also be considered when involvement of the facial bones is present.

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RESTORATION OF THE SELLA TURCICA AFTER TREATMENT OF PITUITARY ADENOMAS*

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AFTER successful irradiation and/or surgical treatment of a pituitary tumor, it is unusual to witness recalcification of eroded sella turcica, dorsum sellae and posterior clinoids. It is even more unusual for an enlarged pituitary fossa to be restored to normal dimensions.

In our experience with 70 patients treated for pituitary adenoma, roentgenographic evidence of sellar reconstruction was noted in only 4 cases, of which 3 (2 chromophobe and 1 eosinophilic adenoma) are to be described in the present communication. The fourth instance was previously reported by our colleagues[1] in an acromegalic who received a tumor dose of 3,000 r. Of particular interest in this case was the reduction in over-all size of the ballooned sella turcica as it recalcified. In the present report, one of our cases also showed a striking reduction in the size of the pituitary fossa, after successful surgical and radiation treatment.

In 1949, Camp[4] stated that when the sella turcica has been decalcified and enlarged by pressure from an intrasellar or extrasellar lesion, and the pressure has been subsequently relieved by one means or another, the margins of the sella turcica may recalcify but the pituitary fossa will not *entirely* return to normal size and shape. Camp further stated that a roentgenogram in such cases will always reveal the residual evidence of an active disease process.[5] This observation has been well supported by the documented experience of other authors as well as by our own. It seems appropriate to review briefly the cumulative reports on this problem from other clinics. Hurxthal, Hare, Horrax and Poppen[10] reporting in 1949 on the treatment of 29 acromegalics, cite 8 patients who showed recalcification—the highest incidence yet reported. However, Kerr[12] observed only one such case in 50; Aitken and Pohle[2] found only one case in 36; Dyke and Davidoff[6] and Gray and Newell[7] each reported a single case. In Camp's patient the recalcification of the sella turcica occurred after surgical removal of the pituitary tumor.[5] Johnsen mentioned 3 cases in a group of 23 acromegalics who developed recalcification and 3 additional cases which exhibited a diminution in the size of the sella turcica.[11] Von Poswick also reported a patient with sellar reconstruction but in his case the sella turcica had been destroyed by a metastatic deposit from a malignant neoplasm.[15] In a textbook by Pendergrass *et al.*[14] there is illustrated a recalcified sella turcica following removal of a meningioma; another in a child irradiated for carcinoma of the hypophysis and sphenoid sinus; and a third in a case (reported by Oldberg[13]) following release of increased intracranial pressure by means of a Torkildsen procedure. This was a nineteen year old woman who had cerebral manifestations for a year and a half. Pneumoencephalography performed in 1942 disclosed marked internal hydrocephalus of the lateral and third ventricles. No evidence of a neoplasm could be found at surgical exploration. In 1944, she was re-admitted at another institution where the reconstruction of the sella turcica was noted. Fortunately, an autopsy was obtained which established the diagnosis of internal hydrocephalus secondary to atresia of the aqueduct of Sylvius. This is one of the few rare instances of a benign lesion giving rise to an enlarged sella turcica.

To stress further the relative infrequency of restoration of the sella turcica, Bachman and Harris[3] pointed out that in none of their 64 treated patients with pituitary

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FIG. 1. Case 1. Before radiation therapy (January 27, 1955). Lateral view of the skull showing enlarged pituitary fossa with thinning of the floor, dorsum sellae and posterior clinoids. (The insert shows the sella turcica measurements in millimeters.)

adenomas have they seen an enlarged sella turcica decrease in size or demineralized clinoids show evidence of recalcification. It appears, therefore, that a report of our 3 cases is well indicated.

REPORT OF CASES

CASE 1. F.M., a forty-one year old white salesman, noted blurring of vision in the left eye three months prior to his admission to the hospital. He presented a bitemporal defect in visual fields in addition to decreased visual acuity in the left eye. Blood sugar, spinal fluid,

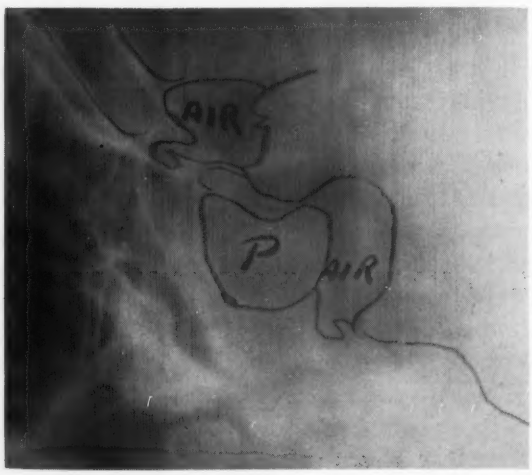

FIG. 2. Case 1. Pneumocisternogram (February 23, 1955) showing protrusion of sellar mass through diaphragma sellae (retouched to show cisterns and pituitary mass P).

FIG. 3. Case 1. After surgery and radiation therapy (July 12, 1956). Follow-up roentgenogram showing recalcification and reconstitution of the floor, dorsum sellae and posterior clinoids. Note smaller pituitary fossa.

I^{131} uptake, routine blood and urine analysis, basal metabolic rate, and total ketosteroids were all within normal limits. Skull roentgenograms on January 27, 1955 showed an enlarged pituitary fossa with demineralization of the bony structures (Fig. 1). A pneumocisternogram obtained on February 23, 1955 revealed the pituitary fossa to be enlarged, with a mass breaking through the diaphragma sellae (Fig. 2). Clinical opinion supported the presence of an intrasellar lesion, probably a chromophobe adenoma, pressing on the optic chiasm and producing the bitemporal hemianopsia.

On March 10, 1955 the subtotal removal of 15 gm. of pituitary tissue was accomplished and a histologic diagnosis of chromophobe adenoma was established. On March 30, 1955 visual field studies were already normal. From April 4, 1955 until April 29, 1955 a course of high energy rotational therapy was delivered to the pituitary fossa. The physical factors were 1,000 kv., 3 ma., 1 mm. Pb filter, half-value layer 3.9 mm. Pb, target-axis distance 70 cm., 6×6 cm. portal. A tumor dose of 3,000 r was given in twenty-six over-all days. The patient has remained well to date. On July 12, 1956 (Fig. 3) skull roentgenograms showed recalcification of the structures in the sella turcica and reduction in the anteroposterior dimensions as well as in the depth of the pituitary fossa. On July 2, 1957 no further change was observed.

CASE II. V.B., a twenty-five year old white

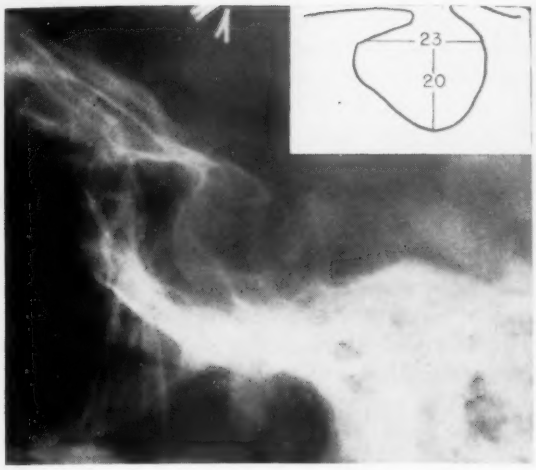

Fig. 4. Case II. After surgery and before radiation therapy (November 17, 1953). Lateral view of the pituitary fossa showing enlarged sella turcica, marked irregularity and thinning of the floor, dorsum sellae and posterior clinoids.

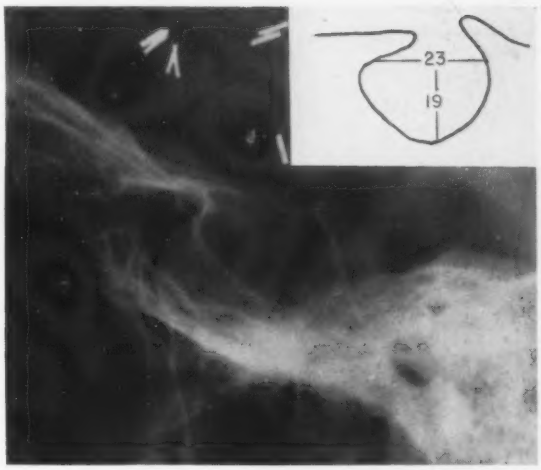

Fig. 5. Case II. After radiation therapy (September 13, 1956). Follow-up lateral view showing marked reconstitution of the floor with recalcification and reconstitution of the dorsum sellae and posterior clinoids (the two latter findings are better visualized on the actual roentgenogram than on the reproduction).

male, was admitted on September 9, 1953 with a history of headaches and blurred vision of five weeks' duration. He exhibited bilateral papilledema with no gross visual defects, and a normal endocrine status. Roentgenograms of the skull on November 17, 1953 showed moderate enlargement of the pituitary fossa and erosion of the floor, with thinning of the dorsum sellae and posterior clinoids (Fig. 4). A right carotid angiogram showed lack of filling of the anterior cerebral artery. Ventriculography revealed poor filling of the anterior portion of the third ventricle as well as the anterior horn of the right lateral ventricle. The clinical opinion supported the diagnosis of a right frontal lobe tumor.

On September 16, 1953 a right frontal craniotomy was performed and a large cyst was exposed in the region of the sella turcica. The cystic lesion was aspirated and a segment of tumor tissue (5×2×3 cm.) was removed from below the right optic nerve. A histologic diagnosis of chromophobe adenoma was established. A course of high energy radiation therapy was initiated, delivering a tumor dose of 2,800 r in twenty-eight over-all days. The physical factors were identical with those employed in Case I, except for the use of two stationary opposing portals of 6×6 cm. each. On September 13, 1956 skull roentgenograms showed recalcification of the posterior clinoids, dorsum sellae and floor of the fossa (Fig. 5). When last seen on July 12, 1957, the patient was in good health and no further changes were noted in the skull roentgenogram.

Case III. M.L., a thirty-five year old white male, first developed enlarged hands and feet in 1942. He was asymptomatic until 1953 when he started to have some loss of vision. During the next two years his loss of vision increased and, in addition, he had progressive loss of strength, and a diminished libido which finally made him seek medical advice. Upon admission he was noted to have acromegalic features of his face, skull, hands and feet, and an upper dorsal kyphosis. The laboratory studies showed a mild diabetic tendency, normal complete blood cell count and an I^{131} uptake which was interpreted as being in the low normal thyroid range. A skull roentgenogram on May 6, 1955 showed enlargement of the sella turcica with a very irregular floor (Fig. 6). There was also thinning of the dorsum sellae and posterior clinoids. A pneumocisternogram on May 9, 1955 revealed no evidence of extrasellar extension of the pituitary tumor. Visual field studies disclosed a marked defect in both temporal fields. The clinical diagnosis was eosinophilic adenoma of the pituitary gland and the patient was referred to the Radiation Therapy Department for treatment. This was done from May 24, 1955 to June 15, 1955

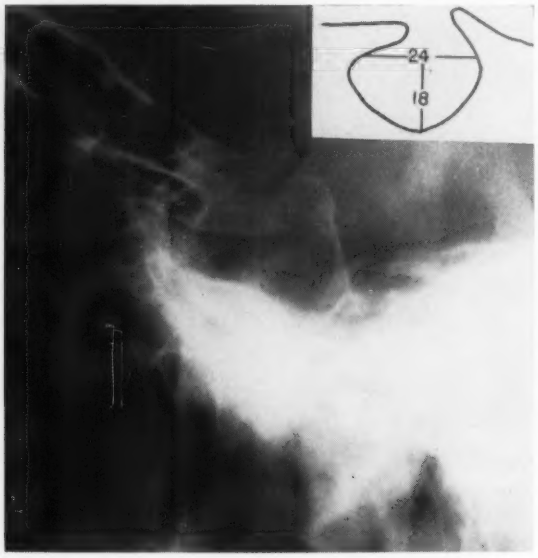

FIG. 6. Case III. Before radiation therapy (May 6, 1955). Lateral view of the skull showing marked enlargement of the sella turcica with marked irregularity and thinning of the floor, dorsum sellae and posterior clinoids.

through a 5×5 cm. portal with 360° rotation on a 1,000 kv. apparatus having a half-value layer of 3.9 mm. Pb. A dose of 3,000 r was delivered in three weeks. During irradiation his visual fields remained unchanged. He was then discharged to our follow-up clinic. Subsequent visits showed some return of his peripheral vision, and, when he was re-admitted on May 22, 1958 because of postprandial epigastric pain, his visual field examination was normal.

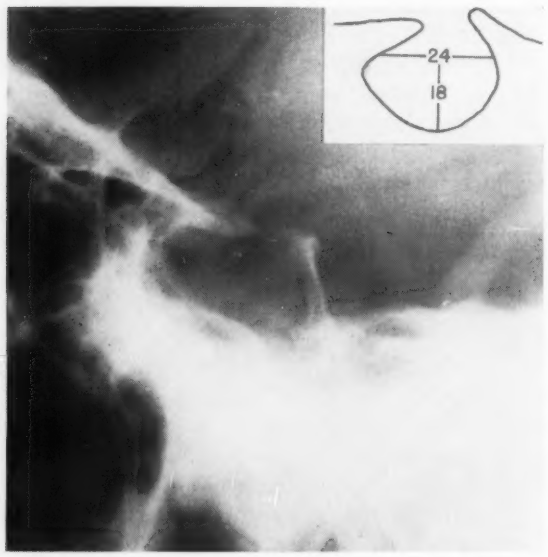

FIG. 7. Case III. Follow-up view of the pituitary fossa (May 22, 1958) showing marked recalcification and reconstitution of the dorsum sellae and posterior clinoids. The floor, however, still shows some irregularity.

At this time, however, he had two nodules in a slightly enlarged thyroid gland. Iodine^{131} studies showed a normally functioning gland. A glucose tolerance test was normal. His skull roentgenogram on May 22, 1958 (Fig. 7) showed marked recalcification and reconstitution of the dorsum sellae and posterior clinoids. The floor was relatively unchanged. He still had loss of his libido, his acromegalic features were prominent, and there was no regression of the enlarged soft tissue. A partial thyroidectomy on August 11, 1958 showed cystic colloid benign adenomas.

SUMMARY

1. Recalcification of the eroded sella turcica, dorsum sellae and posterior clinoids after irradiation and/or surgical treatment for pituitary tumors appears to be an unusual finding. Even more unusual is a reduction in the size of the enlarged pituitary fossa.

2. The published reports of such roentgenographic changes after therapy have been collected and reviewed.

3. Three additional cases have been presented from our experience, making a total of 4 observed in the treatment of 70 patients with pituitary adenoma in our own radiation clinic. Two of these patients had histologically proved chromophobe adenomas, and received surgical and radiation therapy; the third was clinically diagnosed as an eosinophilic adenoma and received radiation therapy. The fourth individual (previously reported) was an acromegalic who was treated with radiation.

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PANTOPAQUE VENTRICULOGRAPHY IN THE LOCALIZATION OF SURGICAL LESIONS OF THE POSTERIOR FOSSA*

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ALTHOUGH neuroradiologic contrast techniques have achieved great precision in the localization of supratentorial neoplasms, they have been less accurate for lesions of the posterior fossa. In many instances, the diagnosis is actually made by exclusion, rather than by demonstration of the lesion. A patient who has symptoms and signs suggesting an infratentorial lesion undergoes pneumoventriculography. The examination shows dilatation of the lateral and third ventricles without distortion, but often no filling of the caudal ventricular system;* occasionally, the beginning of the aqueduct is visualized in the lateral projection and appears to be kinked forwards. The diagnosis of posterior fossa tumor is made and exploration is carried out. If the lesion is visible on the surface, the problem of localization is solved. If not, then investigation of the interior of the cerebellar hemispheres, vermis, or fourth ventricle must be made, with resultant increase in morbidity and mortality.

In a large series of pneumoventriculograms reported by Davidoff and Epstein,[5] utilizing laminagraphy, the fourth ventricle was filled in approximately 40 per cent of the cases. The proximal aqueduct was visualized in about 60 per cent of their cases. In the anteroposterior projection, lateral shift of the aqueduct and fourth ventricle was demonstrated only 7 per cent of the time.† Their illustrations show that the fourth ventricle was not completely filled in most instances.

The figures for fractional or controlled pneumoencephalography are no better. In a series of 24 brain tumors in which there was nonfilling of the ventricles, Ruggiero[12] found that 80 per cent were located in the posterior fossa. In a recent series of fractional encephalograms made at the Mount Sinai Hospital, New York, employing a technique which produces filling of the fourth ventricle in almost every case of nontumor or supratentorial tumor, the results for verified posterior fossa neoplasms were as follows (21 cases): In 66 per cent there was no ventricular filling, in 10 per cent poor filling of the fourth ventricle, and in 24 per cent satisfactory filling of the fourth ventricle. If the acoustic neurinomas (a group in which the diagnosis may usually be made on the basis of clinical and plain roentgenographic examination) are deleted, then in only 12 per cent was there satisfactory filling of the fourth ventricle. Since in several instances an unsuccessful pneumoencephalogram preceded a successful one, or several unsuccessful ones were carried out, the percentage of satisfactory studies in this group was considerably less than 12 per cent.

The pneumoencephalogram demonstrates indirect evidence of a posterior fossa mass lesion in the form of tonsillar herniation, narrowed infratentorial cisternae, and subarachnoid air distribution suggesting hydrocephalus.

Efforts to demonstrate the ventricular system by pantopaque injected into the lumbar subarachnoid space and run upwards with the patient on his back[10] have failed to improve these figures. Such studies give good visualization of the cisternae and

* This term is used to describe the aqueduct and fourth ventricle.

† The proportion of midline and laterally placed lesions is not given.

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are helpful in the diagnosis of angle tumors.

Vertebral angiography has not been of much help in the precise localization of posterior fossa lesions, except in the few cases in which a "stain" has been demonstrated.

In view of the striking need for adequate visualization of the caudal ventricular system, it is of interest that as early as 1928 Balado[2,3] succeeded in filling the fourth ventricle in the presence of posterior fossa lesions by means of positive contrast substance introduced into the lateral ventricle. Yet the procedure has never become popular, being employed sporadically. Bull[4] and Sutton[13] illustrated some examples in which the technique might be applied but did not recommend its routine use. As recently as 1956, Horowitz found it necessary to defend the method and he states that it should never be considered a replacement or an alternative to gas ventriculography.

Some explanation for the reluctance to employ this method is to be found in objections to some of the positive contrast media. This is apparently justified in regards to lipiodol and possibly thorotrast,[1,8] but the evidence adduced for pantopaque as a noxious agent is far from convincing. Thus the presence of pantopaque globules in areas of arachnoiditis cannot be taken to indicate that this substance is the responsible agent.[6,14] Bacterial contamination during lumbar puncture or improper cleaning of detergents from syringes may be at fault.[15] Recently, pantopaque has been used to outline the third ventricle in human stereotaxic surgery without complication.[16] Pantopaque has been used at the Mount Sinai Hospital for many years. It has frequently been run into the posterior fossa to demonstrate the foramen magnum and cisternae. It has now been used for ventriculography for two years. Aside from occasional transient meningeal reaction, such as is seen with air, we have not been convinced of any deleterious effects attributable to the pantopaque.

When it is considered that the use of pantopaque has permitted visualization of the fourth ventricle in almost every case of obstructing or expanding lesion of the posterior fossa; that this procedure is far superior to air studies conducted either from above or below, and easier to perform and less hazardous than pneumoventriculography; that the percentage of real or attributed reactions to pantopaque is a small fraction of a per cent, then it will be readily appreciated that the use of pantopaque for as serious a surgical lesion as that of the posterior fossa is fully justified. In our hands it has proved to be the procedure of choice in the localization of these lesions.

TECHNIQUE

The purpose of the maneuvers to be described is to cause the pantopaque which has been instilled into the lateral ventricle to pass into the third and then the fourth ventricles. This is done by first having it pool in the frontal horn. Then with extension of the head, the medium will pass backwards and drop through the foramen of Monro to the floor of the third ventricle. In order to pass the pantopaque from the third to the fourth ventricle without losing it into the subarachnoid space, it is advisable to turn the patient over on his back so that the pantopaque pools on the roof of the third ventricle. Then by gentle flexion of the head, the pantopaque may be made to completely fill the fourth ventricle.

Whereas previous methods have relied upon fluoroscopy or serial roentgenography[7,9] to follow the course of the pantopaque through the ventricular system, we find this to be unnecessary and time consuming. By following the procedure to be described below, we have been able to fill the caudal ventricular system in every instance within one to two minutes.

Three cubic centimeters of pantopaque are injected into the lateral ventricle through a burr hole. If posterior burr holes are placed in the semisitting position and the patient transported to the radiologic department on his back, then the head must be rotated to bring the pantopaque in-

to the frontal horn. The head should be rotated away from the ventricle containing the pantopaque so that it runs along the septum pellucidum rather than into the temporal horn where it may be trapped. Young children may be somersaulted. If the posterior burr holes are placed with the patient prone (or the pantopaque is added after the patient is in this position), then the medium will usually course forwards into the frontal horn. Assurance of pooling all of the pantopaque in the frontal horn is obtained by placing frontal burr holes with the patient in the prone position, injecting the substance and transporting him to the radiologic department in this position. We usually, but not always, inject about 30–40 cc. of air at the time that the pantopaque is introduced, for reasons given below.

With the patient lying prone on the roentgenographic tilt table and the pantopaque pooled in the frontal horn, the maneuver for advancing it into the third and fourth ventricles may be easily carried out (Fig. 1*A*). The operator stands above the patient's head with a hand on each cheek. He gradually extends the head until the orbitomeatal line is parallel to the floor, or the orbital end of the line is slightly higher (Fig. 1*B*). To do this, it may be necessary to tilt the table up slightly or to arch the patient's back. This allows the pantopaque to pass back on the floor of the frontal horn and to drop through the foramen of Monro

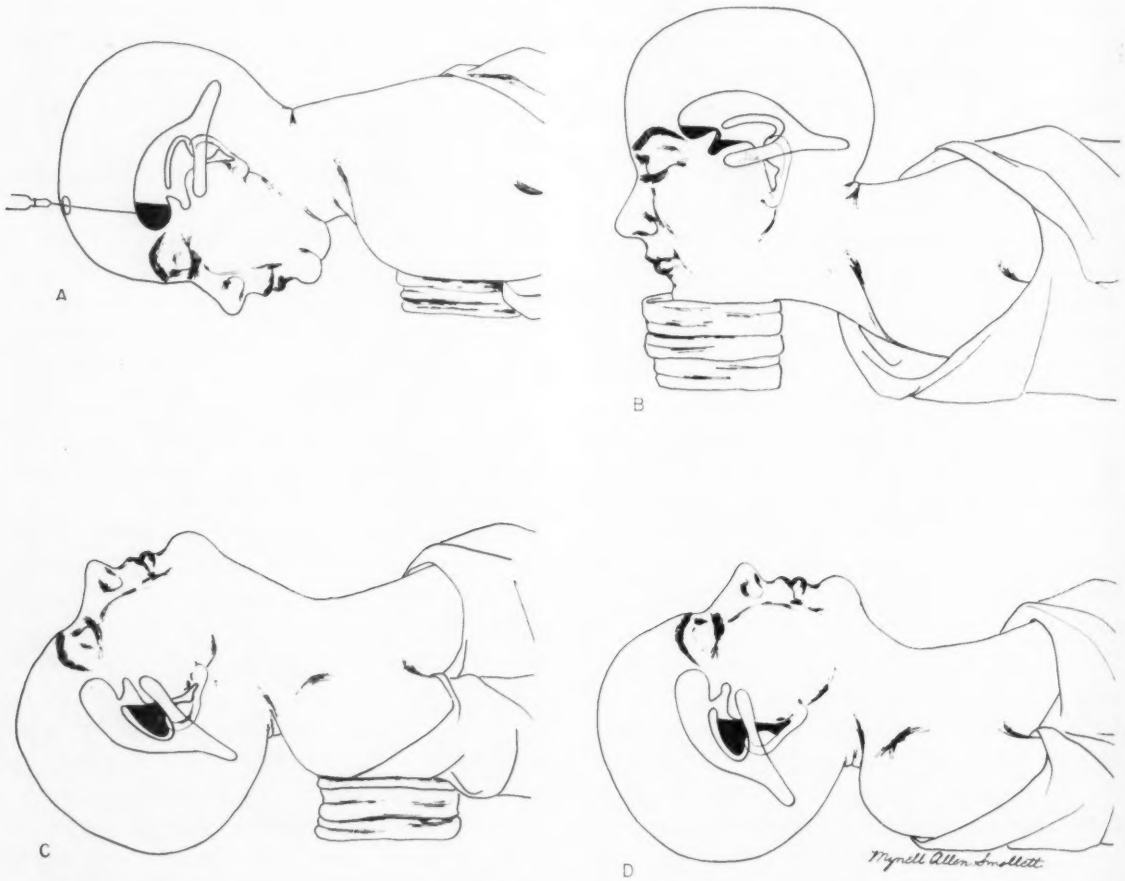


FIG. 1. (*A*) Introduction of pantopaque through a frontal burr hole with patient in prone position. For other methods, see text. (*B*) Extension of head to allow passage of pantopaque into third ventricle. (*C*) Patient turned on back with head maintained in position indicated to allow cradling of pantopaque in posterosuperior third ventricle. (*D*) Almost complete correction of head extension to allow passage of pantopaque into fourth ventricle. Patient in position for roentgenographic studies.

into the inferior third ventricle. Too rapid extension with the head slightly rotated may cause some of the opaque medium to bypass the foramen and pass up over the thalamus into the posterior lateral ventricle. If the extension is too extreme, then pantopaque which has previously entered the third ventricle may pass into the aqueduct and drop through the fourth ventricle into the spinal subarachnoid space.

After this maneuver, the patient is turned supine. The operator maintains firm control of the slightly extended head and rotates it, as two assistants turn the trunk (Fig. 1*C*). If the head is overly extended, some of the pantopaque will reflux through the now dependent foramen of Monro. If it is strongly flexed, the pantopaque will pass through and out of the fourth ventricle. The head is then flexed somewhat so that the orbitomeatal line is slightly less than vertical to the floor (Fig. 1*D*). Following this, anteroposterior and lateral exposures are made.

If this technique, a modification of Lysholm's,[9] is followed, the pantopaque will almost always be found in the third and fourth ventricles. A single roentgenogram will demonstrate air in both frontal horns of the lateral ventricle, indicating the degree of hydrocephalus; air in the anterior third ventricle; pantopaque in the posterior third ventricle; and pantopaque in the fourth ventricle. In the rare instance in which the lesion is about the third ventricle rather than in the posterior fossa, the simultaneous visualization of anterior and posterior third ventricle, as well as the normal fourth ventricle, makes the distinction easy.

No fluoroscopy or preliminary roentgenography is needed, the manipulations being carried out in about two minutes. With practice, we have been able to increase the proportion of pantopaque entering the third and fourth ventricles as compared to that remaining in the lateral ventricle so that it is about two thirds of the total.

One problem which may arise if only a small amount of pantopaque enters the dilated third ventricle, and there is a large suprapineal recess, is the loculation of all the medium in the recess, none of it passing into the aqueduct. This happens because the opaque medium passes along the roof of the ventricle in the supine position to the recess, remaining there when the patient is turned prone. Under these circumstances, it is necessary to turn the patient back to the prone position and flex the head so that the pantopaque drops out of the suprapineal recess into the anteroinferior third ventricle. The head is then slowly extended so that the pantopaque passes back on the floor of the third ventricle to the aqueduct. This must be done slowly to avoid losing the pantopaque down the vertical aqueduct and fourth ventricle. It is safer to pass the medium from the third to the fourth ventricle with the head lateral, and to laterofiex the head towards the ceiling.

Three initial roentgenograms are taken, one in the Waters', one in a 30° Towne, and one in a lateral position across the table. The Waters projection, being predominantly at right angles to the aqueduct and fourth ventricle, tends to show these structures in their long axis. If a less angulated view is desired, a base roentgenogram of the skull can be made later. The Towne projection helps to separate the ventricular system from the surrounding bony structures (of less importance in pantopaque ventriculography) and to give a cross section of the fourth ventricle. A more perfect cross section can be obtained with a 50° Towne projection, if this is desired.

Oblique exposures of the fourth ventricle may occasionally be of value. Finally, if necessary, right and left lateral exposures can be made by rotating the head to the lateral position. This has the advantage in that each side of the fourth ventricle can be visualized separately, but, as it permits pantopaque to flow out of the dependent foramina into the subarachnoid space and to pass back into the third ventricle and from the third ventricle into the dependent lateral ventricle, it should be delayed until the end of the examination.

Another advantage of the small amount of air introduced is that the lateral ventricles may be rapidly screened at the end of the procedure. It is of interest to know whether there is an elevation of the tentorium by posterior fossa tumor (as indicated by upwards displacement of the temporal and occipital horns), tumor springing from the tentorium and growing above and below it, or whether there are supratentorial lesions associated with posterior fossa metastatic disease.

THE RETAINED INTRAVENTRICULAR PANTOPAQUE

In lateral lesions of the posterior fossa, the pantopaque usually passes rapidly out of the fourth ventricle, with some delay if the tonsils are herniated and approximated when the patient assumes the erect position. It drops directly into the spinal canal. The greatest degree of arrest has occurred with midline lesions blocking the caudal ventricular system, such as aqueductal occlusion or tumor of the fourth ventricle. Even here, what seems to be a complete block is usually not, and the pantopaque ultimately passes through. This is somewhat analogous to the situation in myelography when, for example, a thoracic tumor shows a complete block. Should cisternal pantopaque injection be done to show the upper pole of the tumor and the patient sent to the radiologic department in the sitting position, the substance will frequently be found to have completely passed the block. It is surprising how many so-called complete blocks may be overcome by placing the contrast medium in full column above the lesion for a period of time.

The pantopaque which has not entered the third ventricle is also usually expelled from the ventricular system as judged from the postoperative roentgenograms. Every time the patient bends his head down, it runs into the frontal horn, and when he straightens up, he repeats the maneuver for introducing the medium into the third and fourth ventricles. Over a period of time, most, if not all, of the pantopaque is eliminated from the ventricular system in this fashion, whether or not the block was relieved by surgery. It can then, if desired, be removed by lumbar puncture.

RESULTS

With the technique described above, it was possible to delineate the caudal ventricular system in over 30 cases with surgical lesions of the posterior fossa. Of the expanding lesions, all but one showed satisfactory filling of the posterior third ventricle, aqueduct and fourth ventricle. The single exception, in which the fourth ventricle failed to visualize, was a hemangioblastoma of the vermis, recurrent after ten years. These findings suggest that the failure to visualize with air is not due to collapse of the fourth ventricle or occlusion of the aqueduct by the mass, but rather the inadequate contrast afforded by gas. In the case of lesions producing primarily an obstruction of the caudal ventricular system without expansion, it was found that occlusion of the aqueduct was regularly associated with a block of this structure and a failure to fill the fourth ventricle. This latter structure was often filled by pneumoencephalography (Fig. 5, *E* and *F*).

The technique permitted differentiation of obstructing and expanding lesions. In obstructing lesions, the site of blockade could be demonstrated. In expanding lesions, it could be determined whether the lesion was in the midline or lateral to it: in the midline lesion, whether it was supraventricular (superior and inferior vermis), intraventricular, or infraventricular (pontine and prepontine); in the laterally located lesion, whether it was supraventricular (superior and inferior cerebellar hemispheric), paraventricular, or infraventricular (cerebellopontine angle).

The characteristic distortions of the caudal ventriculogram produced by the lesions described above will be the subject of another communication. However, a few examples will be given here to show the accuracy afforded by the method.

For purposes of comparison, a normal

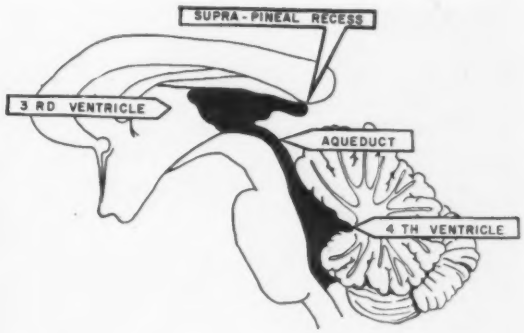


FIG. 2. (*A*) Normal lateral pantopaque ventriculogram. In this case filling was accomplished by the lumbar route in a patient without intracranial disease. Note normal defect in inferior fourth ventricle due to vermis and cerebellar tonsils. (*B*) Tracing of *A*.

pantopaque caudal ventriculogram is included (Fig. 2, *A* and *B*, and *C* and *D*). Note in these and in subsequent illustrations that in the accompanying tracing, the pantopaque is represented exactly as it is seen on the ventriculogram. However, for simplicity, only that pantopaque which is in the posterior third ventricle, aqueduct and fourth ventricle is traced.

The caudal ventriculogram shown in Figure 2 was obtained by running the pantopaque up from the subarachnoid

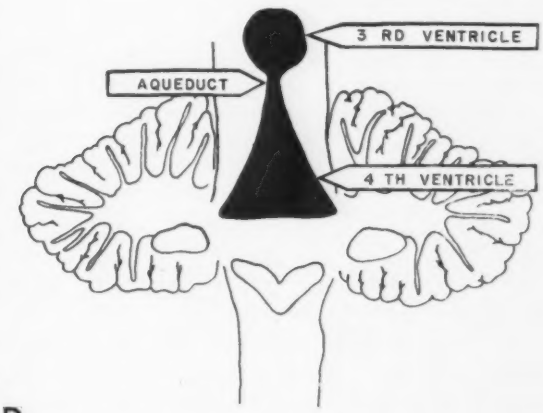
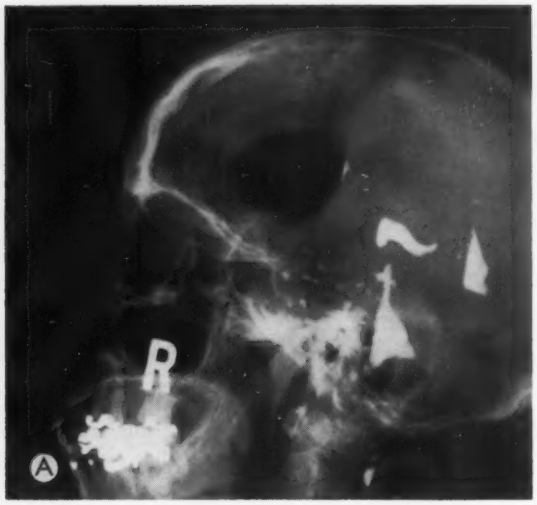
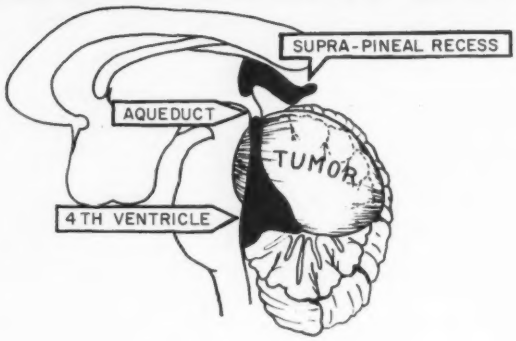


FIG. 2. (*C*) Normal anteroposterior pantopaque ventriculogram. Note well-defined lateral recesses. (*D*) Tracing of *C*.





B

FIG. 3. Expanding lesion, supraventricular, lateral-dorsal. Hemangioblastoma of the superior portion of the right cerebellar hemisphere. (*A*) Displacement of aqueduct and fourth ventricle towards clivus without alteration in shape of fourth ventricular triangle. (*B*) Tracing of *A*.

space following lumbar puncture by the technique described by Mones and Werman[10] in a patient with no intracranial disease. As indicated previously, this technique is suitable for the demonstration of normal anatomy and in some cases of angle tumors and pontine gliomas, but it is unsuccessful in most other posterior fossa tumors. Several measurements have been devised to determine the normal position of the fourth ventricle in the posterior fossa.[5,11,13] These include distance of rhomboid fossa to clivus, rhomboid fossa to fastigium, and fastigium to occipital bone posterior to the foramen magnum. There are many variables in these measurements and any one of them by itself may be highly misleading.

Figure 2, *A* and *B* shows the normal aqueductal curve and fourth ventricle in relation to the clivus. The normal shape of the fourth ventricle is seen with one of its common variations, an inferior filling defect due to vermis, tonsils and possibly also to choroid plexus. Figure 2, *C* and *D* shows the same structures in the anteroposterior projection. Note the appearance of the fourth ventricle as a tall isosceles triangle and the well defined lateral recesses.

Figure 3 shows, for comparison, the caudal ventriculogram in a case with an expanding lesion in the posterior fossa. In the lateral view (*A* and *B*) the aqueduct and fourth ventricle are kinked towards the clivus, indicating a lesion which is supraventricular (or posterior) to the fourth ventricle. The fact that the normal fourth ventricular triangle is preserved indicates that the lesion is not midline but probably lateral in the cerebellar hemisphere. The anteroposterior roentgenogram (*C* and *D*) shows a shift of the aqueduct and fourth ventricle, confirming the lateral location of the lesion. The depression of the basal angle of the fourth ventricle on the side of the lesion suggests that the process is high up or superior in the hemisphere. At operation, a hemangioendothelioma was found in the anterior superior portion of the right cerebellar hemisphere.

The characteristic caudal ventriculogram of an expanding lesion in another compartment of the posterior fossa is illustrated in Figure 4. The lateral projection (*A* and *B*) shows that the normal triangle of the fourth ventricle has been severely disrupted, indicating a lesion in the midline. The proximal aqueduct is visualized and is very dilated, suggesting an intraventricular mass, as lesions above or below the ventricle tend to compress it. In addition, small globules of pantopaque are seen anteriorly and low in the fourth ventricle. In the anteroposterior projection (*C* and *D*), the third ventricle and a small portion of anterior fourth ventricle are seen to be undisplaced, confirming

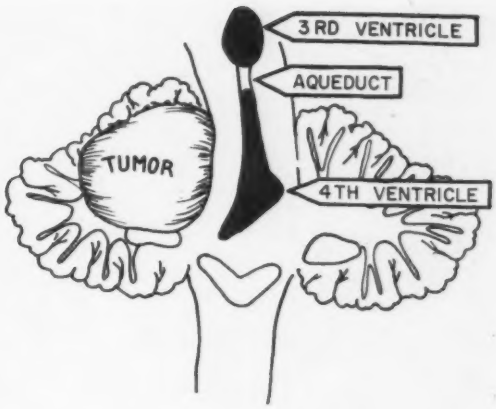


FIG. 3. (*C*) Marked shift of aqueduct and fourth ventricle away from tumor. Note depression of ipsilateral basal angle of fourth ventricle suggesting a dorsal lesion. (*D*) Tracing of *C*.

the impression of a midline lesion. Droplets and crescents of pantopaque can be seen passing down around the right border of the tumor only. In a later film, these all collected in a midline, inferior fourth ventricle. The impression from the films was a mass in the superior portion of the fourth ventricle. At operation, an astrocytoma was found in this region.

Figure 5 illustrates an entirely different type of surgical lesion of the posterior fossa. In *A* and *B* a tapering aqueduct is seen, with no filling of the fourth ventricle, such as is observed characteristically in aqueductal occlusion. The normal curve of the aqueduct with lack of displacement towards or away from the clivus is also in favor of this diagnosis. In *C* and *D* the aqueduct and third ventricle are noted to be in the midline. The fourth ventricle is again not visualized. The diagnosis is confirmed in *E* and *F*, where air has been injected by the lumbar route and a laminagram taken. It shows a normal fourth ventricle and together with the pantopaque delineates the site of obstruction.

This study made it unnecessary to explore the posterior fossa for tumor.

DISCUSSION

The localizing value of pantopaque ventriculography for infratentorial lesions having been established, the question may be raised as to whether it is the primary procedure to be employed in patients suspected of harboring a surgical lesion of the posterior fossa. We feel that this is not the case, and that fractional or "controlled" pneumoencephalography should be done first. This procedure, which consists of the injection of 10 to 15 cc. of gas via the lumbar route with the withdrawal of minimal or no fluid, has been shown to be safe in a large number of cases[12] and was used in a majority of our patients. In individuals not harboring a surgical lesion, the fourth ventricle and cisternae will be filled, thereby obviating the need for burr holes and ven-

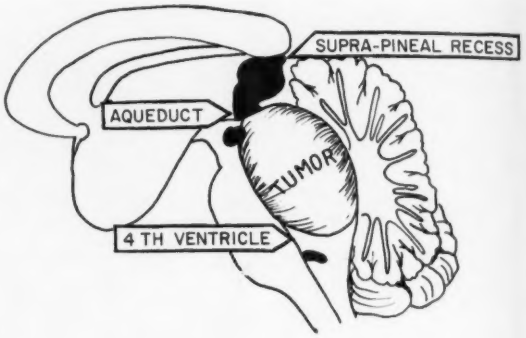
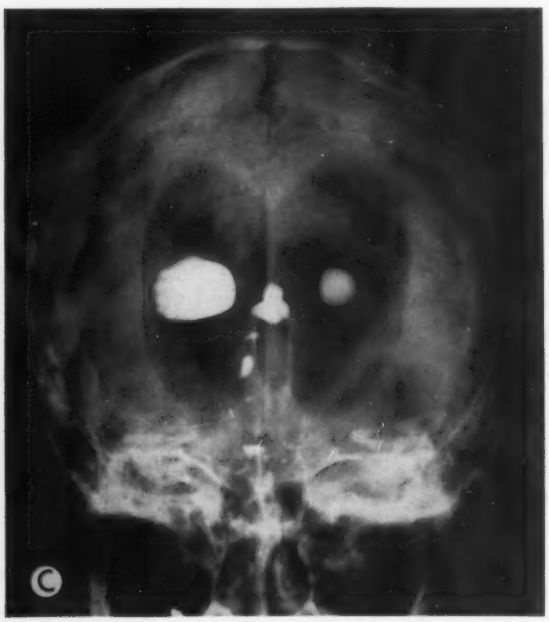


FIG. 4. Expanding lesion, intraventricular. Astrocytoma of the superior fourth ventricle. (*A*) Almost complete cut-off of dilated aqueduct close to its origin. Note widening of aqueduct as block is approached. Droplets of pantopaque anterior and caudal to tumor. (*B*) Tracing of *A*.

tricular tap. In those cases of "pseudotumor cerebri" which are clinically indistinguishable from a posterior fossa tumor, the attenuated ventricles will usually fill, thereby not only preventing an unnecessary ventriculogram but also the trauma occasioned by trying to tap very small ventricles. The procedure will also serve to disclose clinically mislocalized supratentorial masses and, in cases of aqueductal occlusion, a normal fourth ventricle with block of the aqueduct.

In a small percentage of cases, adequate amounts of air will enter the ventricular system and permit an exact localizing diagnosis. Even if there is no filling, indirect diagnosis of an unlocalized lesion of the posterior fossa may be made by findings of tonsillar herniation, small cisterna magna and pontine cistern and increased arching



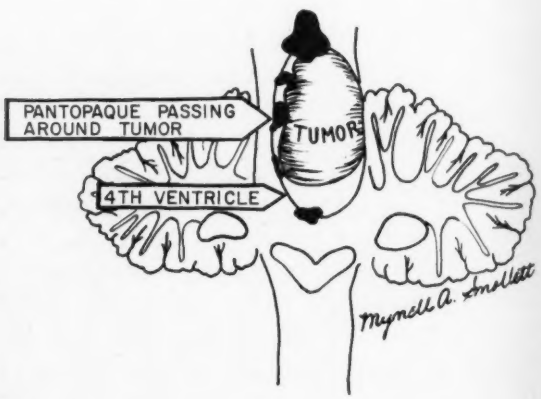
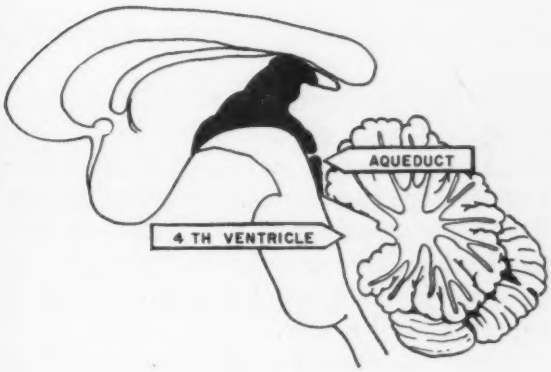
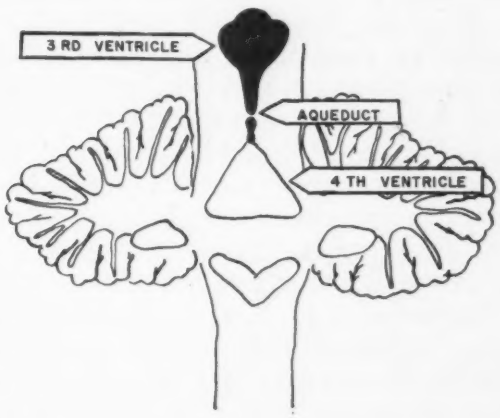


FIG. 4. (*C*) Essentially midline position of third ventricle and inferior fourth ventricle, while pantopaque deviates laterally around right side of tumor lying between these two points. (*D*) Tracing of *C*.



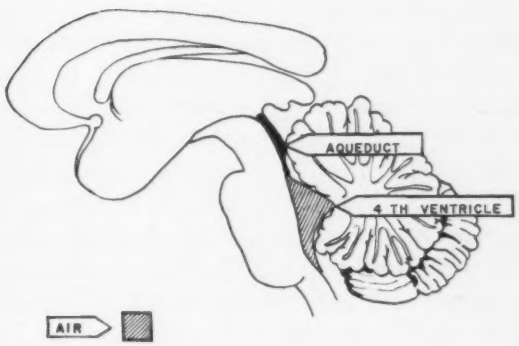
B

FIG. 5. Obstructing lesion. Aqueductal occlusion. (*A*) Fourth ventricle not seen (as is the rule in aqueductal occlusion). Normal aqueductal curve progressing to tapering block distally. (*B*) Tracing of *A*.



D

FIG. 5. (*C*) Absence of filling of fourth ventricle. Aqueduct in midline. (*D*) Tracing of *C*.



F

FIG. 5. (*E*) Laminagram showing filling of normal fourth ventricle by injection of air from below. Pantopaque in aqueduct and air in fourth ventricle come into contact, outlining thin obstructing lesion. (*F*) Tracing of *E*.

of air in the cingulate and callosal sulci, indicating hydrocephalus. Air in the cisterna chiasmatica and interpeduncular cistern helps to rule out suprasellar lesions. The presence of air in the midline in the longitudinal fissure and equally over both cerebral hemispheres helps to exclude a supratentorial tumor.

After fractional pneumoencephalography, the procedure described in this communication should be carried out if a localizing and lateralizing diagnosis has not been made. Other diagnostic measures are available; however, to date they have not been too successful in aiding in the localization of tumors of the posterior fossa.

Of these, the recently introduced technique of pantopaque cisternoventriculography (myeloencephalography [MEG]) via the lumbar route, as described by Mones and Werman,[10] should be mentioned. If air does not enter the fourth ventricle in the preliminary pneumoencephalogram, pantopaque introduced from below is even less likely to do so. However, if partial filling is obtained with air, more precise information may be gained if the fourth ventricle can be filled from below by pantopaque. This is predominantly true in brain stem tumors and angle tumors. This technique gives excellent visualization of the cisterns of the posterior fossa and is probably the most valuable procedure for demonstrating small angle tumors before they have deformed the fourth ventricle.

Vertebral angiography has been disappointing except in those few instances in which there is a tumor "stain," in large aneurysms of the posterior fossa behaving like expanding lesions, and in distinguishing pontine from prepontine lesions. Carotid angiography is helpful in ruling out a cerebral hemispheric lesion. A study of the deep cerebral veins is of value in ruling out a para third ventricular tumor, while confirming the presence of advanced hydrocephalus.

These ancillary procedures have a definite place in the diagnostic work-up and should be utilized whenever the information they provide is required for adequate localization.

SUMMARY AND CONCLUSIONS

1. Currently employed contrast studies, whether air introduced into the ventricular system or into the lumbar subarachnoid space, posterior fossa cisternoventriculography from below with pantopaque, or vertebral angiography are usually inadequate for the precise localization required for surgical lesions of the posterior fossa.

2. These methods (excluding vertebral angiography) fail because of their inability to demonstrate the fourth ventricle.

3. Pantopaque when introduced into the ventricular system permits visualization of the fourth ventricle in almost every instance. This is accomplished rapidly and *without the need for fluoroscopy or preliminary roentgenography*. The distortion of the caudal ventricular system thus demonstrated provides a precise preoperative localizing diagnosis. When combined with a small amount of air, the completeness of the study is enhanced.

4. No adverse effects due to intracranial pantopaque, other than transient meningeal reaction, have been noted in a large series of cases.

5. Pantopaque ventriculography should replace pneumoventriculography in the roentgen diagnosis of surgical lesions of the posterior cranial fossa.

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CISTERNAL PNEUMOENCEPHALOGRAPHY*

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PNEUMOENCEPHALOGRAPHY, introduced by Dandy[1] in 1919, is one of the pillars of neurologic and neurosurgical practice. Yet, as it is commonly performed by the injection of 60 or more cc. of air into the lumbar subarachnoid space, it is one of the more unpleasant diagnostic procedures in routine clinical use, and both the increasing reliance upon carotid angiography and the present interest in radioactive isotope studies in the localization of brain tumors indicate a certain dissatisfaction with the method as it is currently employed.

In the early 1930's, injection of about 150 cc. of air and withdrawal of all available cerebrospinal fluid (with the patient sitting up) was a fairly standard procedure. The type of reaction following such lumboencephalography may be judged by Grant's[5] article of 1932, in which he stated "Following encephalography we have frequently seen patients so severely shocked that immediate operation was out of the question" and ". . . if a tumor can be located . . . the reaction following the injection of air . . . may be fatal." The shortcomings of this type of examination are obvious, and it was early realized that the symptoms and complications were very much reduced if a small amount of air was used. In 1931 Laruelle,[8] for example, advocated the use of not much more than 10 cc. by the lumbar route. It was also known by that time that if air were injected directly into the cisterna magna by suboccipital puncture, a more selective filling of the ventricles could be obtained than by the lumbar route. Flügel[4] advised the use of about 20 cc. of air in this manner and employed it successfully in patients with intracranial tumors (though without papilledema).

Nevertheless, small, selective pneumographies were not generally accepted and many neurosurgeons settled independently for about 60 or 70 cc. injection of air by the lumbar route. Perhaps the wide acceptance of Davidoff and Dyke's[2] text-book is one reason for the present popularity of such a procedure.

It has long been known that intracranial tumors are diagnosed by distortion of the ventricle pattern, not by distortion of the air distribution over the cortex. The diagnosis of some tumors by means of a "telltale" cortical bubble has been described but we do not know of any in which such a diagnosis was made in the presence of a completely normal ventricular pattern. It has also long been known that the capacity of normal ventricles is about 18 to 20 cc. of fluid;[2] it would seem, therefore, that the problem is to introduce 18 or 20 cc. of air selectively into the ventricles except that in the case of suprasellar or parasellar tumors a few more cubic centimeters must be directed into the basal cisterns. Air over the cortex is painful and unnecessary.

Robertson[11] is one of those who in particular has constantly sought to improve the technique by the selective placement of small volumes of air (lumbar route) rather than by simultaneous total visualization of each and every cerebrospinal fluid space. Later, Kristiansen and Vogt,[7] and Lindgren[9] advocated very similar methods. A very small amount of air, 5 or 10 cc., is first introduced. Roentgenograms are taken and the head then altered in position, if necessary, to direct further air anteriorly or posteriorly by extension and flexion, respectively. By selective distribution of the air, excellent visualization can be obtained by 25 or 40 cc. in the majority of cases. Though more time and care are certainly required in the performance of this technique and in its interpretation, the greater

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comfort of the patient makes such considerations irrelevant.

Many series have been reported. One of the most recent is that of Norlén and Wickbom.[10] They did 140 fractional pneumographies in patients with tumor but without papilledema. Two patients deteriorated as a result of the procedure. They had a further series of 82 patients with tumor and papilledema of whom 4 deteriorated. One patient died, probably as a result of the test, but it is not stated in which series. They believe that pneumoencephalography and angiography are the procedures of choice in the contrast diagnosis of the majority of supratentorial tumors, that pneumoencephalography is of great value in outlining tumors of the basal cisterns and in the cerebellopontine angle, but that ventriculography is necessary in a large proportion of cerebellar tumors (23 out of 36 cases).

To return to the view of Flügel[4] and earlier workers that selective filling of the ventricles is more satisfactory if the suboccipital route is used, we find that the idea, though dormant, was not entirely abandoned. Jefferson[6] is one of those who advocate it, stating "it upsets the patient less and the ventricles are filled more easily." The reason why the ventricles fill more easily is that the air is injected directly into the cisterna magna and its easiest outlet, in the vertical position, is into the ventricles. It does not escape into the anterior basal cisterns. Air injected into the lumbar space, on the other hand, ascends both in front of and behind the cord (Fig. 1), enters fairly easily into the anterior basal cisterns, and thence spreads over the cortex. If in an effort to prevent this anterior escape the head is flexed too much, it will escape posteriorly over the cerebellum so that the optimum position of the head has a narrow range. If a patient develops headache and is restless, this optimum position is extremely difficult to maintain.

At the present time many prefer suboccipital pneumoencephalography in the presence of normal intracranial pressure, but there is a growing belief that it is preferable to, and safer than, ventriculography in cases of raised intracranial pressure (except in those cases of tonsillar herniation where, of course, the method is impossible). Of 189 patients with brain tumor subjected to ventriculography by Dressler and Albrecht,[3] 9.52 per cent died, and there was a deterioration in 15.3 per cent. Following suboccipital encephalography in 193 similar patients, death occurred in only 1 (0.52 per cent), and deterioration in 2.59 per cent. If we consider only those patients in whom papilledema was present, the figures do not differ greatly. Following ventriculography (131 patients) 11.45 per cent died and a further 12.98 per cent deteriorated. Following suboccipital pneumoencephalography (104 patients) 0.96 per cent died and 2.88 per cent deteriorated. We cannot understand, nor do the authors explain, the extremely high mortality and morbidity figures following ventriculography. They are somewhat higher (though not much

Fig. 1. Air is ascending in neck from lumbar injection. Head is in neutral position, air ascends in front of and behind the cord. A small amount of air enters the prepontine cistern and the cisterna magna.

higher) than the figures quoted by Grant[5] in the early 1930's, but the low figures after cisternography even in the presence of papilledema are impressive. It seems improbable that puncture of the brain alone could cause the high mortality in ventriculography. It may be that larger volumes of air are used in standard ventriculography than in suboccipital pneumography, and it may be that the sudden raising and lowering of intracranial pressure to which the patient is subjected may be a further deciding factor.

MATERIAL

During the past year we have performed 118 pneumographies in patients with a wide variety of neurologic disorders, mostly to diagnose or exclude intracranial tumors. Patients with papilledema were investigated by ventriculography or arteriography (except 2 who had suboccipital pneumoencephalography). Forty-six of the 118 patients had pneumography by the lumbar route; in 72 the cisternal approach was used. There was no selection in this distribution except that more patients were done cisternally as our confidence increased.

TECHNIQUE OF CISTERNAL PNEUMOENCEPHALOGRAPHY

We had noted that Dressler and Albrecht[3] performed the cisternal puncture with the patient in the supine position, occasionally supported on his elbows and with the head flexed. We thought this was not only cumbersome but subject to danger if the patient for any reason ceased to support himself, and we placed the patient sitting on or astride an upright chair with the back vertical and the head flexed. In this position the needle is horizontal or even tilted down and our filling was unsatisfactory for two reasons. In the first place, some air did not enter the ventricles but escaped over the posterior cerebellum; and, secondly, when we disconnected the syringe it was possible for some air to escape back through the needle. We then realized that Dressler and Albrecht's[3] head position was the proper one and by providing a comfortable reclining chair solved the difficulty of support. The patient reclines on a chair thrown well back and flexes his neck (Fig. 2). Reid's base line lies horizontally and it is possible to direct the needle upward instead of straight in. This upward direction of the needle has the further advantage that if inserted too far it would continue upward into the cistern rather than horizontally through the spinal cord. The site of the mid-line puncture is above the spinous process of the axis which is at the level of the tip of the mastoids. The direction is toward the glabella. After injecting local anesthetic, a No. 22 needle is advanced until it engages into the thick drum-like atlanto-occipital membrane. The point of the needle is now no longer free but is tightly gripped by this membrane. It is then advanced 1 mm. beyond the membrane. If intracranial pressure is not increased, fluid will not flow out freely. To verify the position of the needle, one aspirates with a light 1 cc. syringe. If no fluid is obtained, the needle may be advanced a further millimeter and another attempt made. It is rarely necessary to advance beyond this. A cisternal puncture is easier to perform than a lumbar puncture. With the head flexed the suboccipital space is wider than the interspinal space. If at the depth of 2 mm. beyond the atlanto-occipital membrane no fluid is obtained, then one obeys the absolute unyielding law of cisternal puncture—in the presence of any problem or difficulty, desist. There is no place for inspired poking; there is no second try in cisternal puncture. Either the needle is unskilfully directed and is not in the cisterna magna at all, or it is there impinging the cord or herniated tonsil. It should be withdrawn immediately. The beginner who has difficulty in finding the atlanto-occipital space should initially aim high, then step down the occiput with the needle (the area being well anesthetized) until he finds the membrane. Beyond the membrane he too has only one try. When, with a little experience, a three dimensional mental image of

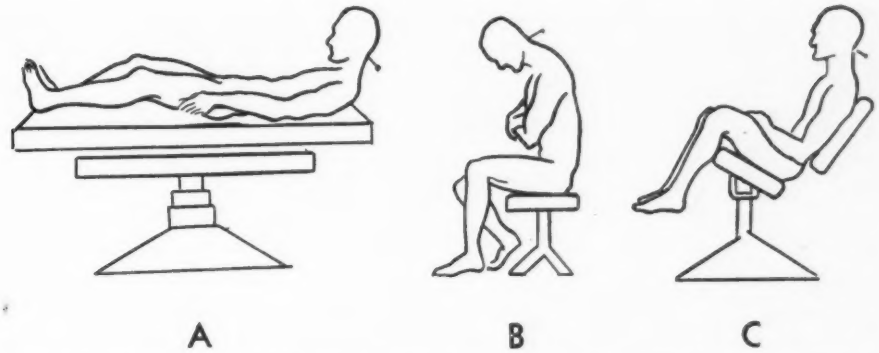

FIG. 2. (*A*) Dressler and Albrecht's[3] position. Needle points up. (*B*) Wrong position. Needle points down. (*C*) Correct position. Needle points up and in spite of moderate flexion of neck, Reid's base line is horizontal.

the cisterna magna has been acquired, a single gentle puncture is all that is ever needed. When the position of the needle is verified by aspirating one drop of fluid, air is slowly introduced over a period of three to five minutes. If there is not a free flow of air or fluid through the needle at any time during the procedure, it may be felt that the needle has been inadvertently withdrawn. This is a dangerous assumption because it might equally well have been inadvertently advanced. Therefore, always withdraw the needle completely through the atlanto-occipital membrane and reposition it rather than advance it by mistake into the cord.

No pain is experienced during the injection of the first 10 cc. of air. If significant pain occurs at this stage, then air is not entering the ventricles and the head must be re-positioned or the examination abandoned. It is best to take roentgenograms and see what actually is happening. There may, for example, be a block of the aqueduct. Between 10 and 20 cc. a mild headache may develop, but rarely of any significance before the 20 cc. mark. If the ventricles are large, no headache develops though large quantities are introduced. In the majority of cases we have not withdrawn fluid until the total air has been introduced, for it has been shown by Ryder *et al.*[12] that readjustment to the previous pressure, whether high or low, is achieved with extreme rapidity. In ordinary cases 20 or 25 cc. are adequate for a satisfactory air study (Table 1). We have, on occasion, used much greater quantities than this, but we do not believe that we have achieved any better filling with large amounts than with small ones except in patients with dilated ventricles. If no headache whatsoever is experienced after 20 cc. of air is injected, it is well to add more air because the ventricles are large and require a greater volume to outline them clearly. As a rule we continue until some headache is experienced. The patient is then placed on his back and routine roentgenograms taken. If air escapes from the ventricular system during positioning of the head, further headache will be ex-

TABLE I

Cisternal Pneumography			Lumbar Pneumography		
Air Injected (cc.)	No. of Cases		Air Injected (cc.)	No. of Cases	
10	1		15– 20	1	
15–20	14		26– 30	2	
21–25	22	52	36– 40	6	
26–30	16		41– 45	4	
31–35	6		46– 50	10	
36–40	8		51– 55	5	37
41–50	2		56– 60	8	
———	3		61– 65	4	
71–75	—		66– 70	2	
Total	72		76– 80	1	
Cisternal	72		96–100	2	
Lumbar	46		106–110	1	
Total	118		Total	46	

TABLE II

CISTERNAL PNEUMOGRAPHY IN INTRACRANIAL NEOPLASM

Case No.	Age (yr.)	Diagnosis	Air Injected (cc.)	Papilledema	Complication
8C	60	parasagittal meningioma	23	no	none
13C	27	temporal lobe cyst	22	no	none
23C	46	squamous cell carcinoma, intracranial	30	yes	fainted
25C	40	glioblastoma	25	yes	none
31C	57	acoustic neurinoma	30	no	none
39C	50	cerebral metastatic carcinoma	35	no	none
46C	49	frontal astrocytoma	25	no	none
50C	44	oligodendroglioma	30	no	none
55C	75	sphenoid ridge meningioma	25	no	none
63C	63	glioblasto-astrocytoma	25	no	none
69C	68	parietal meningioma (heart failure, early)	20	no	none

pected. In most patients headache has fairly completely subsided within a few hours after the procedure unless the patient is restless and spills air into the subarachnoid spaces. It was our impression that patients with tumor had less headache than the others.

RESULTS

By both lumbar and cisternal routes we had less than 10 per cent unsuccessful or unsatisfactory ventricular filling. The cisternal failures occurred in earlier cases when we were still improving our technique, particularly that of position. If the cisternal puncture proved unsuccessful we have not repeated it, but on the same or subsequent day have done a lumbar examination (not always with success). In 11 of our suboccipital pneumographies, intracranial neoplasms were present (Table II). Only 2, the squamous cell carcinoma and the glioblastoma, had papilledema, but in none of the total 72 patients in this series was there any deterioration whatsoever.* Three of the patients did not have an operation, including the patient with squamous cell carcinoma who had papilledema (Fig. 3). In the 8 who came to surgery, the operation in each instance was at the time of election and was in no way precipitated by pneumography. The patients included a seventy-five year old woman and a case with mild heart failure. The only complication beyond mild headache occurred in the patient with

FIG. 3. Intracranial extension of squamous cell carcinoma. Note the erosion of the temporal bone on the right. The right ventricle did not fill. Thirty cubic centimeters of air were used and, though the patient fainted during the injection, he had practically no headache afterward. Marked papilledema was present.

* One patient in a subsequent series with an, as yet, undiagnosed degeneration temporarily worsened after cisternal pneumoencephalography.

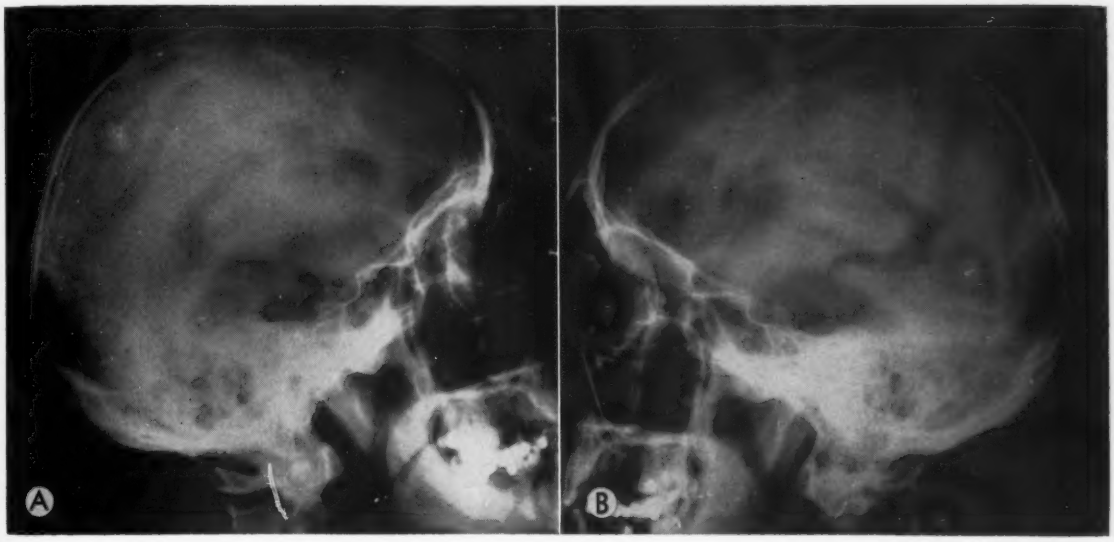

Fig. 4. (*A* and *B*) Large left temporal lobe cyst. No papilledema. Twenty-two cubic centimeters of air were used.

the squamous cell carcinoma, who fainted for a few seconds during the injecting, but peculiarly enough was one of those who had virtually no headache. He had 30 cc. of air. Most striking result of the study, apart from the safety in cases of intracranial tumor, is the relative mildness of the procedure. A patient, 13C (Fig. 4, *A* and *B*), who had a temporal lobe cyst, was sitting up in bed calling for breakfast and a newspaper within ten minutes after the end of the study, completely without headache. Another patient, 39C (Fig. 5), had moderate frontal headache during the injection but none immediately afterwards. Shock, profuse perspiration, severe retching and vomiting were absent from this series. A few patients were nauseated at the completion of injection. Headache rarely lasted more than a few hours. In none of those who had less than 30 cc. of air injected did headache persist into the next day. This is in contrast to the findings of Davidoff and Dyke,[2] who found that patients who had on an average 63 cc. of air had symptoms for an average of 2.25 days.

In general, the patients having selective lumbar pneumographies had more disturbance. In most of them we used a greater volume of air (for example, 35 to 40 cc.) than in the suboccipital cases (Table 1). Nevertheless, these patients, too, suffered less than did those in whom we used our previously standard method (65 cc.). One patient who had standard pneumography a year previously commented after a small lumbar study, "My, you've taken the kick out of this thing."

In one case of aqueduct stenosis in an adult, in whom tonsillar herniation was subsequently shown at autopsy, an at-

Fig. 5. Left occipital metastatic tumor. No papilledema. Thirty-five cubic centimeters of air were used. Note filling of the total ventricular system (including third and fourth ventricle) except in the neighborhood of the tumor.

tempted cisternal puncture was unsuccessful, but the patient suffered no consequent deterioration. It is noteworthy that in this patient with long standing tonsillar herniation, the atlanto-occipital membrane was extremely thin. It was quite unlike the normal thick drum-like membrane but rather like the lumbar dura and just gave enough sense of resistance to known when it was punctured. The normal atlanto-occipital membrane, on the other hand, requires a deliberate but controlled effort to penetrate it. One must remember this possibility of a thin membrane and judge one's position by depth as well as by resistance. The cistern is usually encountered at 5 to 6 cm. from the surface.

DISCUSSION

Our present enthusiasm for the cisternal route does not lead us to recommend it for all and every diagnostic air study. We emphasize that the suboccipital puncture is not a procedure for the inexpert. Lumbar pneumoencephalography is more versatile in that the large range of movement of the head during injection allows air to be directed at will over the base (by extension) into the ventricles (neutral) or over the cerebellum (by flexion). One can plan the volume and direction of subsequent air injections by study of the roentgenograms as the procedure advances. Lumbar pneumoencephalography is, therefore, preferable if one wishes to examine the cortical subarachnoid space in cases of atrophy or if one wishes to examine the subarachnoid cisterns in cases of suprasellar, parasellar, or cerebellopontine angle tumors. If one wishes to fill the ventricles, there is the disadvantage that air ascending in front of the cord (Fig. 1) may escape into the basal cisterns. For all cases of suspected supratentorial tumor with normal pressure, which are essentially diagnosed by deformity of ventricular filling, the suboccipital method is that of choice. It may well be that this is also the method of choice in cases of intracranial tumor with raised intracranial pressure, though if tonsillar herniation is present no fluid will be obtained and the method is impossible. Dressler and Albrecht[3] have produced figures indicating that in their hands it is safer than ventriculography, while Jefferson[6] states, "I've become convinced by experience that it is a safe, practicable and advantageous method, the danger of which in skilled hands is more apparent than real," and "I've never seen trouble follow cisternal puncture even when cerebellar tumor was present."

SUMMARY

1. Recent literature in England and in Germany suggests that cisternal pneumoencephalography, using about 20 cc. of air, is preferable to lumbar encephalography and in those cases with raised intracranial pressure, it may be superior to ventriculography.

2. During the last year, 72 suboccipital cisternographies were performed at the University of Chicago Clinics. In 9 of these, intracranial tumors were present though there was no papilledema. In a further 2, intracranial tumors were present with papilledema. No patient suffered any deterioration whatsoever and in no case was operation precipitated by the examination. Headaches in all 72 cases were mild, short-lived and in a few instances almost completely absent. No shock, severe perspiration or retching were encountered. The benign course of patients who had 20 cc. cisternal pneumographies is contrasted with that following a 65 cc. lumbar air injection.

3. We are of the opinion that suboccipital pneumoencephalography is the pneumography of choice in cases of suspect intracranial tumor without papilledema. It is probable that it will also prove to be a procedure of choice in those cases with papilledema. Investigation of the cerebral cortex, basal cisterns, and posterior fossa may be made more conveniently by the lumbar route. In the presence of tonsillar herniation and with cerebellar tumors in general, ventriculography is required. Cisternal pneumoencephalography gives adequate

ventricular filling in the presence of patent pathways. It is less painful than lumbar pneumoencephalography. It is probably less dangerous then ventriculography. It is quicker than ventriculography or selective lumbar encephalography. It possesses the potential hazard of cord or medullary puncture in the hands of the inexpert.

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DYNAMIC ENCEPHALOGRAPHY

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PNEUMOENCEPHALOGRAPHY or encephalography, which was first employed by Dandy[3] in 1919, is a useful procedure in the study of various encephalopathies. The air is usually introduced via lumbar puncture and, for this reason, the method should be avoided in cases of increased intracranial pressure, particularly if marked, because of the danger of cerebellar herniation.

In 1919, Dandy advised against the use of encephalography and even lumbar puncture in cases of increased intracranial pressure produced by cerebral tumors. He felt that these procedures were safe only if decompression had previously been effected by a ventricular puncture. Many investigators[1,7,9,17,18,19,23,24] since have felt that the use of encephalography in cases of increased intracranial pressure should be avoided and for such cases have suggested ventriculography. Davidoff and Dyke[5] performed ventriculography in cases of increased intracranial pressure, and, when this examination proved inadequate, they employed pneumoencephalography but only after burr holes had been made to facilitate a ventricular tap if this became necessary.

We have performed encephalography in cases of increased intracranial pressure since 1948. Undoubtedly, the risk of cerebellar or cerebral herniation in these cases at times is very great, but this has been avoided by the use of a careful technique. We have employed the suboccipital route routinely, rather than lumbar puncture, for the introduction of air.

The cisternal puncture offers two advantages. First, it allows an exact measurement of the pressure of the cerebrospinal fluid in the posterior fossa, and secondly, it enables us to establish beforehand whether the cisterna magna is of normal size or whether it has been encroached upon or completely obliterated. We found that, as we acquired experience with this procedure, this was not difficult to ascertain. The puncture is carried out very slowly, advancing the needle only a little at a time. Thus, it is possible to gauge approximately the "back to front" dimensions of the cisterna magna. This is taken as the distance the needle has advanced from the time the cerebrospinal fluid began to flow to the moment when this flow ceased. In most cases, it is not necessary to advance the needle until its point is obstructed. It is sufficient to know that the cisterna magna is at least 0.5 cm. from back to front. If this procedure is carried out gently and with the utmost care, there is no risk whatsoever.

In cases of increased intracranial pressure, the cisterna magna is progressively encroached upon by the hernia of the vermis and the cerebellar tonsils. For this reason, the point of the needle makes contact with the vermis or the tonsils, and the outward flow of the cerebrospinal fluid through the needle is stopped before the needle has reached the medulla oblongata. In patients with very high cerebrospinal fluid pressure and great reduction of the cisterna magna, we formerly used ventriculography rather than encephalography. In all other cases of increased intracranial pressure where the cisterna magna was partially preserved, we undertook encephalography with good results, not experiencing any accidents. Thus, we performed encephalography with greater frequency (95 per cent of the cases) than ventriculography. From 1948 to 1954 we were guided principally by the size of the cisterna magna rather than by the intracranial pressure in determining which procedure to employ, not only in the posterior fossa lesions but also in cerebral tumors.

In 1949, Lindgren[15,16] described an encephalographic technique with which he obtained good results, even in those patients suffering from increased intracranial pressure. He also employed it effectively in

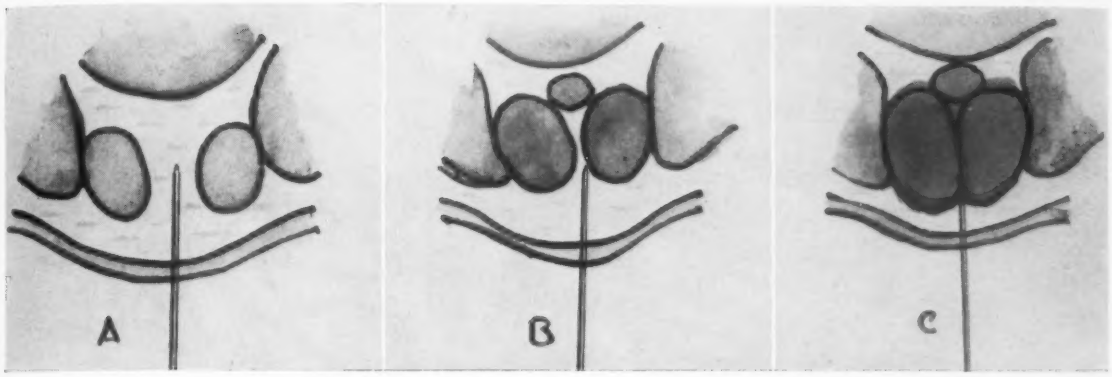

Fig. 1. Sketch of the cisternal puncture. (A) Normal. The cisterna magna is of normal anteroposterior depth. The needle can be advanced unobstructed between the tonsils until it reaches the anterior wall of the cistern (the medulla oblongata). (B) Increased intracranial pressure with moderate cerebellar hernia into the cisterna magna. The hernia of the vermis and cerebellar tonsils occupies part of the cisterna magna. The depth of the cisterna magna and, hence, the distance the needle can be advanced is less than normal. (C) Cases of greatly increased intracranial pressure (marked cerebellar hernia into the cisterna magna). The vermis and the tonsils occupy nearly all of the cisterna magna. The cisterna magna is markedly encroached upon and, hence, the needle can be advanced only a short distance.

cases of cerebral atrophy.[14] In Lindgren's technique the danger of cerebellar and cerebral herniation is eliminated by the use of three fundamental principles: (a) The pressure of the cerebrospinal fluid is kept at a high level; (b) air is injected only 5 to 10 cc. at a time, the location of the air and the patient's condition being carefully evaluated before each increment is added; and (c) the ventricles and the subarachnoid cisterns can be studied after an injection of only 20 to 25 cc. of air by roentgenograms taken in various positions.

Lindgren introduced air by a lumbar puncture, injecting the first 5 to 10 cc. very slowly and without withdrawing cerebro-

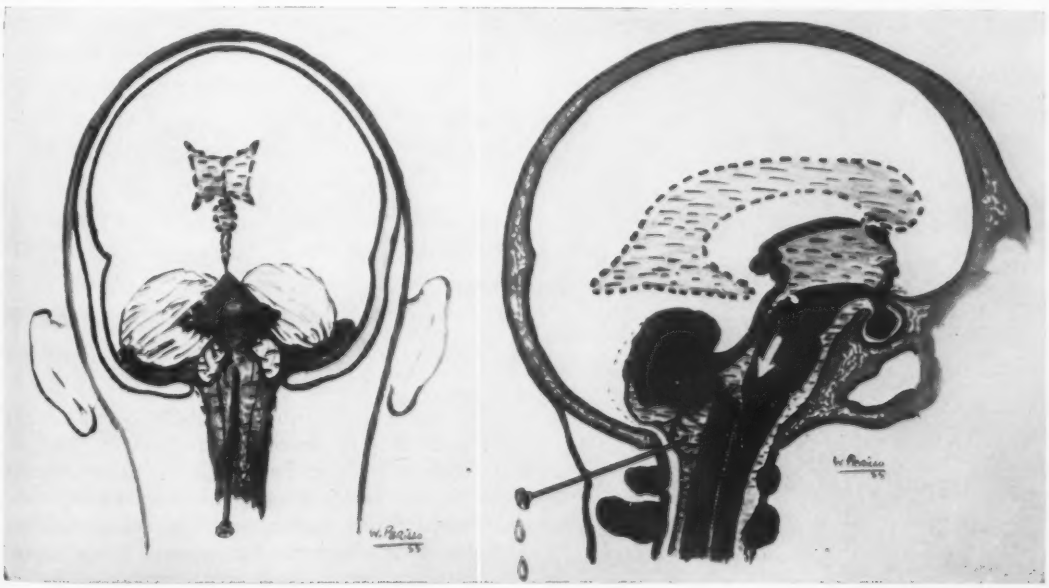

Fig. 2. Sketch showing the position of the needle in the high cisternal puncture. The needle point is placed in the upper part of the foramen mangum between the cerebellar tonsils, the lower ends of which lie below the needle point.

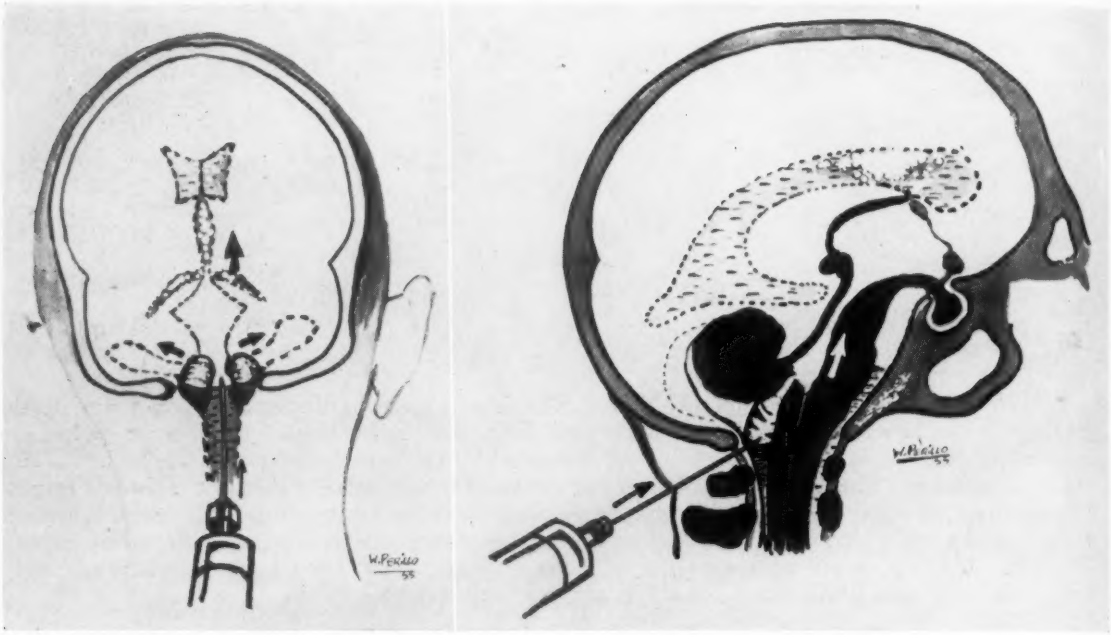

Fig. 3. Sketch showing the modifications produced after the withdrawal of cerebrospinal fluid and the injection of 10 to 15 cc. of gas. The midline ventricular system is filled with gas as well as the basal cisterns. A temporary air-fluid level is produced in the upper part of the foramen magnum, leaving the lower ends of the cerebellar tonsils floating in the cerebrospinal fluid.

spinal fluid; thus, the pressure in the spinal canal was maintained and prevented herniation of the tonsils into the foramen magnum. If air entered the ventricles, further air was injected. The volume of the fluid withdrawn was always smaller than that of the air injected. The position of the head was adjusted in order to obtain about 15 cc. of air in the ventricles, and later some 10 cc. in the cisterns. Lindgren[14] demonstrated that the process is applicable in cases of posterior fossa tumors, and is of greater usefulness than ventriculography because it shows not only the ventricles but also the subarachnoid pathways and cisterns.

Falk[8] confirmed Lindgren's investigations by an analysis of results obtained on 1,800 patients studied in the Department of Radiology of the Serafimerlasarettet during 1948–1951. Falk pointed out, however, that there are risks of hemorrhage and late com-

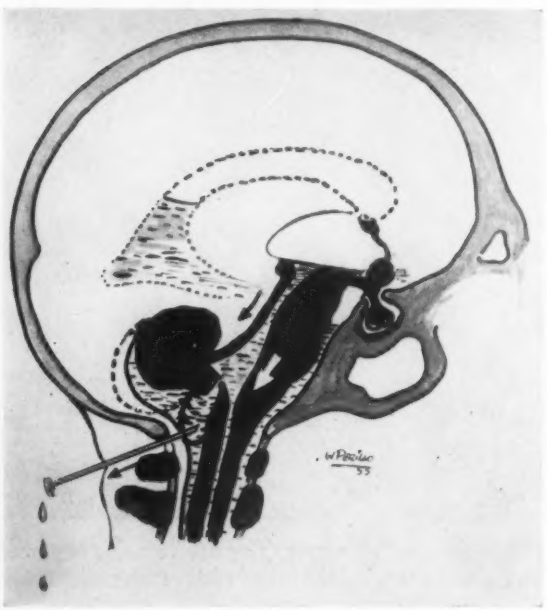

Fig. 4. Sketch showing the outward flow of the cerebrospinal fluid through the puncture needle, after the injection of gas, in a case where the gas flowed freely towards the lateral ventricles. By this means the increased intracranial pressure produced or accentuated by the gas injection is immediately relieved and danger of hernia of the cerebellar tonsils into the foramen magnum is avoided.

plications, such as calcification, associated with the technique. Lindgren's technique also is hazardous in cases of markedly increased intracranial pressure in which central tumors block the third ventricle or the aqueduct and in cases of posterior fossa tumors which block the fourth ventricle. In these cases, the burr holes should be made first in case it becomes necessary to tap the ventricles for decompression.

Wickbom and Sheldon[28] are also in agreement with the results obtained by Lindgren and Falk and stress the great value of the procedure, together with vertebral arteriography, for the diagnosis of posterior fossa tumors. Heppner,[12] describing a case of postventriculography air embolism, points out other likely complications from ventriculography, including infection, cerebral edema, hemorrhages, and hypersecretion of the cerebrospinal fluid. For these reasons he considers Lindgren's encephalography preferable to ventriculography. Ruggiero[25,26] has confirmed Lindgren's work. In his opinion, encephalography carried out with this technique, which he calls fractional encephalography, is no more dangerous than ventriculography and is preferable in a number of respects.

Fig. 5. Sketch showing the outward flow of injected gas and cerebrospinal fluid through the puncture needle in cases where the flow of oxygen is in the ventricular system and is obstructed by a mass lesion of the posterior fossa, the third ventricle, etc. The escape of gas and fluid immediately relieves the increased pressure produced by the oxygen injection and thus relieves the danger of herniation of the cerebellar tonsils into the foramen magnum.

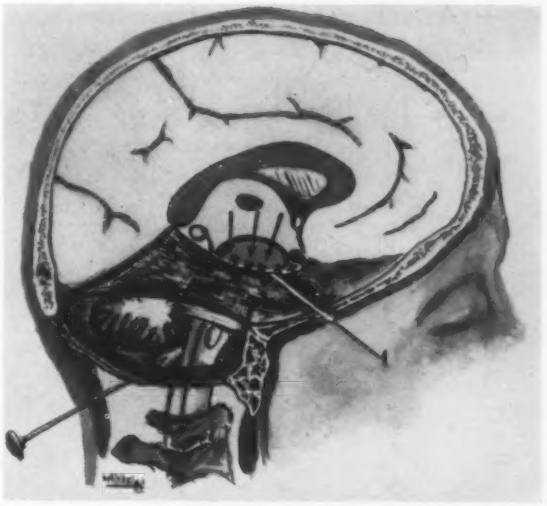

Fig. 6. Sketch showing that the reduction of pressure produced in the posterior fossa by dynamic pneumoencephalography aggravates incipient tentorial cerebral hernias.[3] In these cases, this procedure should be avoided and in its stead ventriculography should be employed.

TECHNIQUE

Since 1953, we have used a technique which we call "dynamic encephalography." This was developed on the basis of our experience with encephalography via the suboccipital route and with Lindgren's technique, which we had also used. In October, 1954, we presented an initial communication to the Neurological and Neurosurgical Society of Uruguay[21] showing the results of our first 7 cases.

The technique is based on the following principles:

1. A high cisternal puncture is made with the needle ascending obliquely. The needle point reaches the cisterna magna at the level of the upper part of the foramen magnum between the cerebellar tonsils. Thus, the lower ends of the tonsils are below the point of the needle.

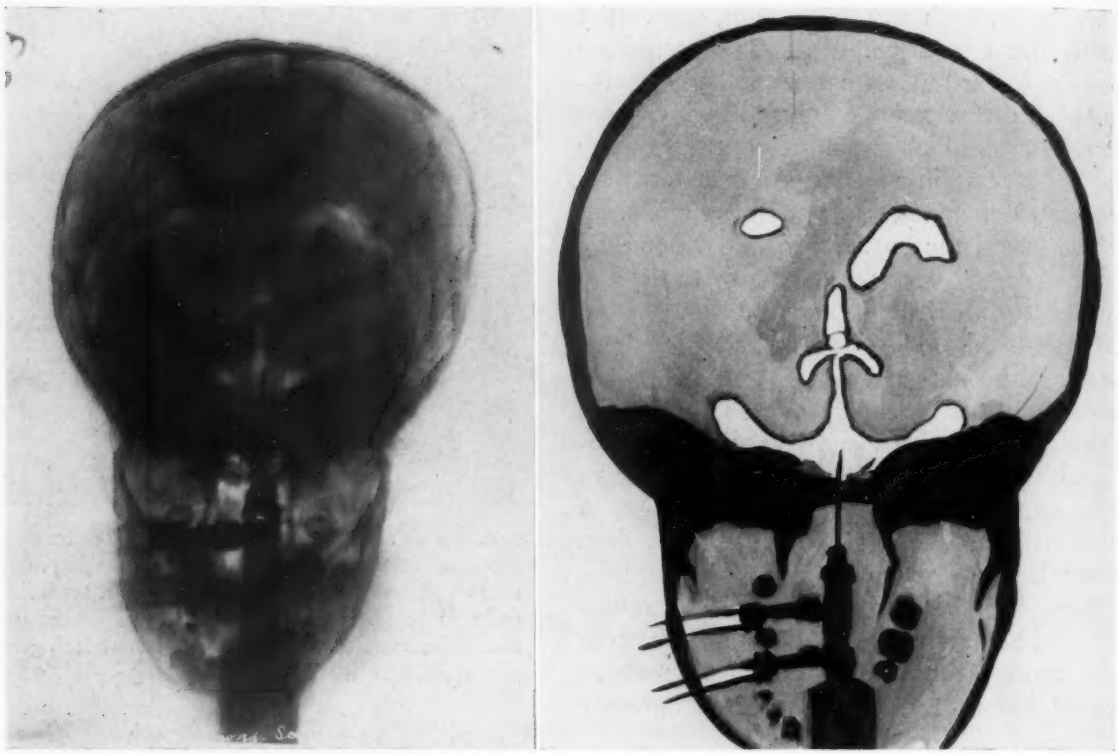

FIG. 7. Dynamic pneumoencephalography (posteroanterior roentgenogram) in a normal case, showing the fourth ventricle, the aqueduct, the third ventricle and the basal cisterns.

2. Under these conditions, when fluid is removed from the cisterna magna and air is injected, the column of cerebrospinal fluid which remains below the needle point and continues to fill the spinal canal along the whole of its length to the foramen magnum supports the cerebellar tonsils.

3. The injection of 10 to 15 cc. of air with the needle in this position, followed by the outward flow of air or cerebrospinal fluid through the same needle, produces an increase in intracranial pressure of very brief duration. Thus, the herniation of the tonsils into the foramen magnum is avoided. This is because (a) the accentuated increase in intracranial pressure lasts only a few seconds; (b) the cerebellar tonsils are supported by the column of cerebrospinal fluid; (c) the decompression produced by the needle is effected at the level of, or just above, the foramen magnum where the cerebellar herniation might occur.

4. In those cases where no obstruction or compression of the fourth ventricle, aqueduct or third ventricle exists, the rapid injection of 10 to 15 cc. of air into the cisterna magna with the patient in a sitting position results in the filling of these structures. At the same time, part of the injected air enters the basal cisterns. Single, or better, serial roentgenograms taken during the final stages of the air injection demonstrate the basal and posterior fossa cisterns, the fourth ventricle, aqueduct, and the third ventricle before the air accumulates in the lateral ventricles.

5. In cases of obstruction or compression of the fourth ventricle, aqueduct or third ventricle, the injection of 10 to 15 cc. of air into the cisterna magna fills only the distal portion of the midline ventricular system up to the site of obstruction and only distends the cisterns of the posterior fossa for an instant, before the air or cerebrospinal fluid escapes through the needle. Conse-

quently, roentgenograms taken during the final stages of the air injection show the distal ventricular system up to the point of obstruction and the cisterns of the posterior fossa and the base.

The technique is carried out as follows: The patient is placed in a sitting position, firmly held, with his head against the roentgenographic plate. The upward puncture of the cisterna magna is performed with a fine needle with a short beveled edge, following local anesthesia with 1 per cent nupercaine. The needle should penetrate the skin precisely in the midline, just above the apophysis of the axis. It is then pointed obliquely upward and forward, and passes just beneath the posterior border of the foramen magnum, to enter the cisterna magna at the level of the foramen magnum. The needle point is then situated in the middle, or even in the superior portion of the foramen, which is really a short bony canal. The pressure of the cerebrospinal fluid in the cisterna magna is measured. The roentgenographic machine is held in readiness while 8 to 20 cc. of oxygen are injected rapidly through the needle and one or more roentgenograms are taken at the precise moment that the air injection is completed. The syringe is promptly removed, leaving the needle in position to allow an immediate escape of injected oxygen or cerebrospinal fluid from the cisterna magna, thus immediately relieving the increased intracranial pressure which has been caused or accentuated by the injection. The injection is repeated with the roentgenograms taken in various positions depending on the case and the indications. The best positions are the posteroanterior and the lateral. It is sometimes necessary to take roentgenograms in oblique positions in order to avoid superimposition of the mastoid images. Later, the usual roentgenograms are taken in order to demonstrate the various parts of the lateral ventricles.

Fig. 8. Lateral roentgenogram in a normal case showing the fourth ventricle, the aqueduct, the third ventricle and the posterior part of the lateral ventricles and the basal cisterns.

RESULTS

We have used this technique on 170 patients to date. The results have been most encouraging so far. The procedure has been well tolerated in nearly all cases. Only one fatal accident, in a comatose woman with multiple metastases, has occurred. In some of the patients we have noted minor complications such as headache, moderate tachycardia, nausea and vomiting.

The roentgenograms have been very good, demonstrating quite clearly the fourth ventricle, the aqueduct, the third ventricle, and the cisterns of the posterior fossa and the base, showing the deformity or displacement of these structures produced by an expanding lesion.

This technique offers a number of advantages over other procedures. It shows up the lateral and midline ventricular system

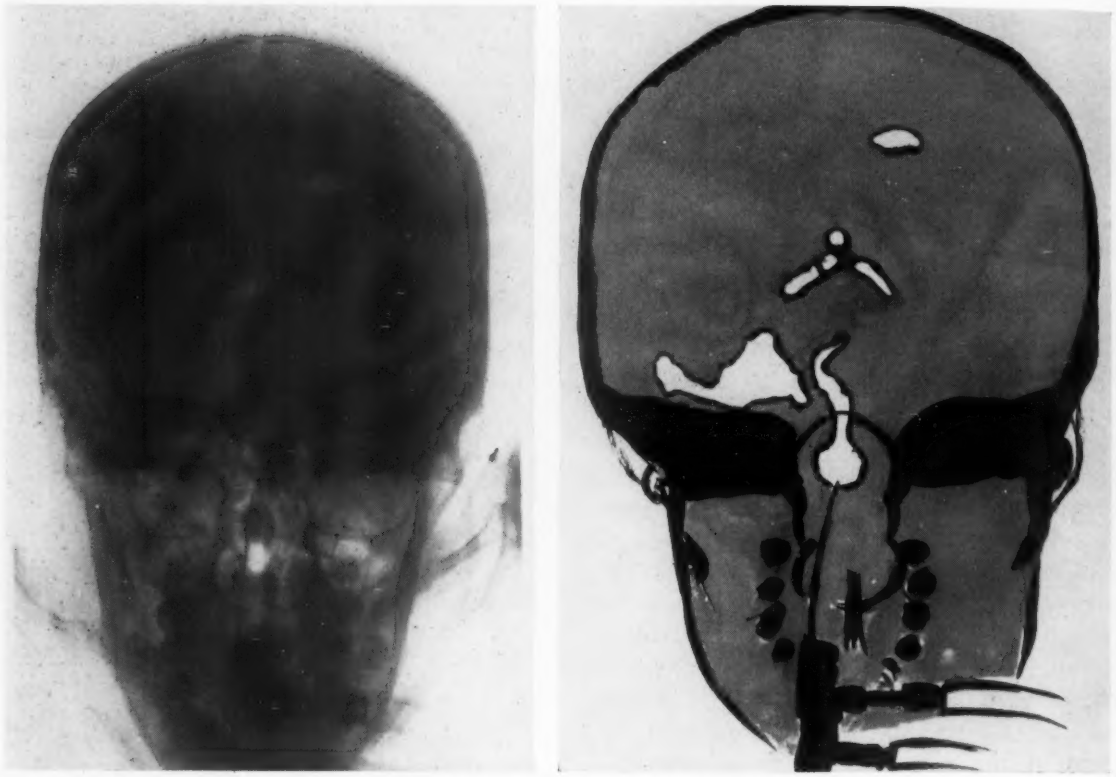

FIG. 9. Large meningioma of the right cerebellar hemisphere. Dynamic pneumoencephalography at a moderate pressure, showing the deformity of the fourth ventricle and the cisterna magna, with the disappearance of the right pontocerebellar cistern.

quite clearly as well as the cisterns of the posterior fossa and of the base. It can be used in most cases of increased intracranial pressure and is most useful for the diagnosis of mass lesions in the posterior fossa. If necessary, the air injections can be repeated several times in order to obtain better roentgenograms in various positions. The procedure requires very little time. It is generally well tolerated by the patients and causes fewer complications than encephalography via lumbar puncture.

In Lindgren's method, the air is introduced into the spinal canal far below the foramen magnum, while in the technique suggested by the author, the oxygen is injected into the cisterna magna itself, above or at the upper edge of the foramen magnum.

With the same needle the posterior fossa is decompressed, and, in this way, the danger of cerebellar herniation into the foramen magnum is minimized.

This technique must only be carried out by experienced individuals. The proximity to the medulla oblongata makes any error potentially hazardous.

In cases of very high intracranial pressure, where danger of a tentorial cerebral hernia exists and has perhaps begun, the process should be supplemented by previous decompression carried out by inserting a cannula into the right lateral ventricle.

The procedure presents no difficulty in most cases of tentorial cerebellar hernia produced by expanding lesions of the posterior fossa inasmuch as the decompression is carried out in the fossa in which the tumor is situated.

SUMMARY

A new method of encephalography is described. It is called "dynamic" because the roentgenograms are taken while the injected oxygen is moving upwards through the ventricular system and also because the

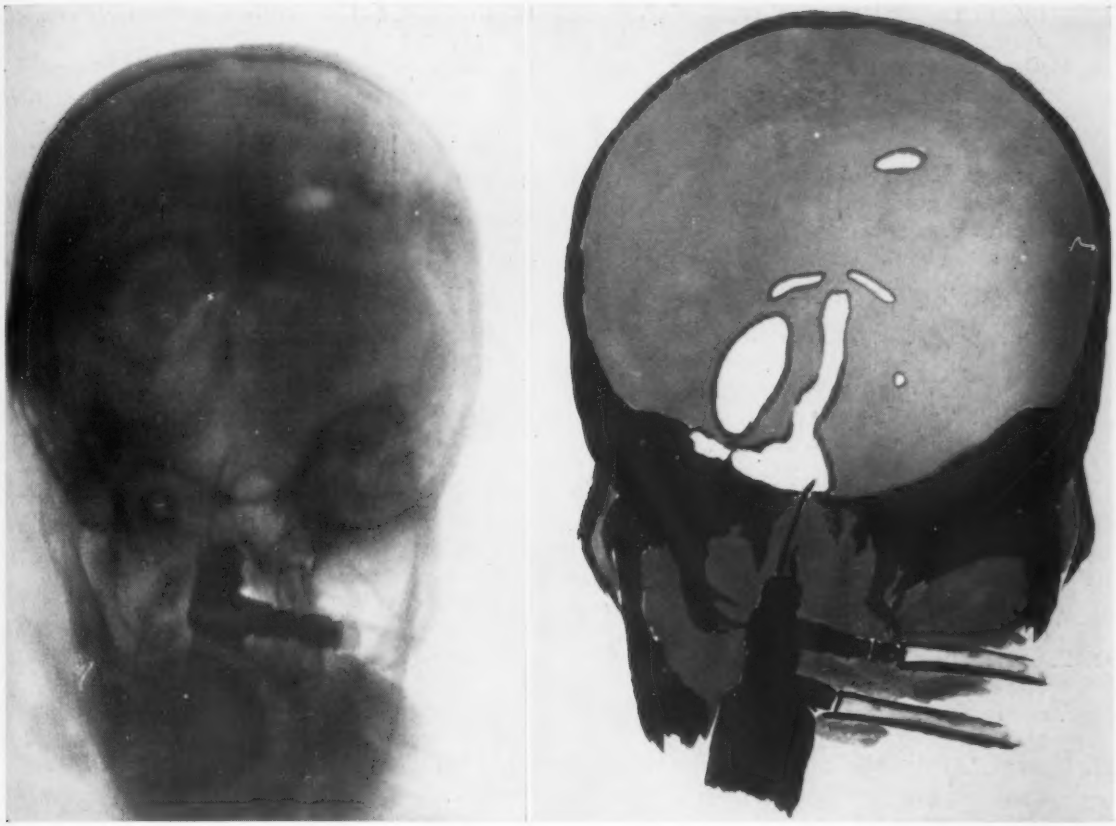

Fig. 10. Large meningioma of the right cerebellar hemisphere. Dynamic pneumoencephalography at a higher pressure shows the expansion of the aqueduct, the deformity of the fourth ventricle and of the cisterna magna. There is nonvisualization of the right hemispheric and pontocerebellar cisterns with complete visualization of these structures on the left side.

cerebrospinal fluid and gas are immediately allowed to flow out.

The procedure which has been used in 170 cases with excellent roentgenographic results is, in general, well tolerated by the patients.

It can be employed in cases of increased intracranial pressure and is very useful when a posterior fossa tumor is present. In cases of increased intracranial pressure when there is danger of cerebral herniation through the tentorium, a decompressing cannula is previously inserted in the right lateral ventricle.

Oxygen is injected by means of a high cisternal puncture with the needle point above or at the upper edge of the foramen magnum and, therefore, above the osseous ring into which the cerebellar tonsils might herniate. By this method, the cerebrospinal fluid column within the spine is maintained and prevents downward herniation of the cerebellar tonsils. Furthermore, as the needle is left *in situ* and permits the escape of gas or cerebrospinal fluid immediately after the oxygen injection, the increased intracranial pressure produced or accentuated by the injection is of brief duration.

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ROENTGENOLOGIC PRINCIPLES OF A NEW STEREOTAXIC APPARATUS*

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THE successful introduction of guided instruments in the brain depends primarily on the proper roentgenologic localization of intracerebral reference points in relation to the zero position of the electrode or needle. When roentgenograms are taken, it is essential to keep the median plane of the skull parallel to the roentgenographic film because only under these conditions all structures in the midsagittal plane of the skull are projected in a constant ratio to the film. In order to insure this position of the skull, various devices are used in the different stereotaxic apparatuses, such as two plastic plates which are placed parallel to a line drawn on the head from the center of the bridge of the nose to the inion.

In the instrument described in this paper, the position is insured by using the roentgenographic guide attached to the apparatus. For that purpose the stem of the guide is provided with a frontal and anterolateral posterior movement which permits correct position that is always parallel to the film.

In choosing the distance of the roentgenographic tube from the film, it should be taken into consideration that even distances of 3 or 4 meters as used by Talairach *et al.*[2] do not make it possible to attain exactly parallel roentgenograms. At a 3 meter distance, for instance, structures in the median sagittal plane of the head are enlarged at the ratio of about 95 to 100. Furthermore, at these distances of the roentgenographic target from the film, it is necessary to use a rather large roentgenographic room. Exact centering is difficult and time consuming, particularly when dealing with patients suffering from involuntary movements. We use a target film distance of 110 cm. and the magnification is calculated by measuring the enlargement of the distance between the center of the spheres in the roentgenographic guide and the same distance in the film. Spiegel and co-workers[1] determine the zero position of the electrode in their instrument by the intersection of the interaural and median plane. It should be noted that the median sagittal plane of the skull and that of the brain frequently do not coincide due to cranial asymmetries or because of pathologic flatness, as in instances of atrophic changes of parts of one hemisphere. Therefore, it is necessary to visualize intracerebral structures such as the septum pellucidum or third ventricle on anteroposterior roentgenograms in order to find the location of the median plane of the brain.

In the instrument described in this report, the zero line is determined automatically by the stem of the roentgenographic guide.

DESCRIPTION

The ideal stereotaxic apparatus should fulfill the three following minimum requirements: (1) The apparatus should be as light as possible and must be attached rigidly to the skull in such a way that the measurements can be taken in exactly the same position when necessary; (2) the electrode holder or needle must have the necessary movements in all three directions in space, including the inclination in the sagittal as well as in the frontal plane, and simultaneously measure the corresponding angles; (3) there must be provisions to position the skull exactly and rigidly for roentgenographic examination so that the median sagittal plane of the skull or preferably the

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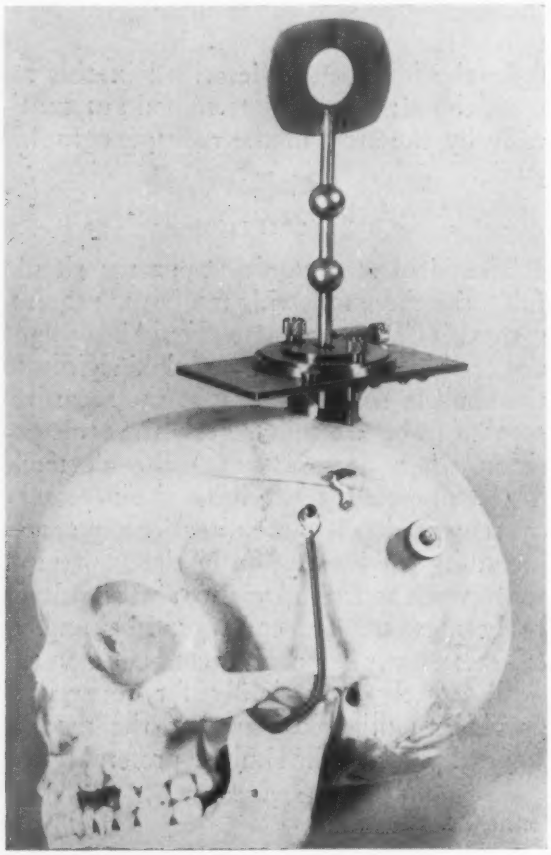
Fig. 1. The platform is attached to the skull by means of inserting the ring into the trephine hole previously made.



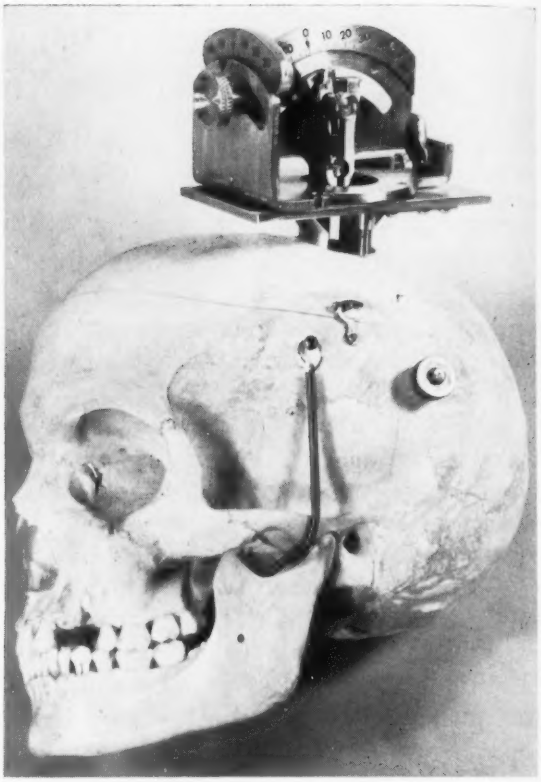


Fig. 3. A needle carrier mounted in the protractors is attached to the platform.

zero line is parallel to or perpendicular to the roentgenographic film.

There has been an attempt to meet the above mentioned requirements in the apparatus which I have developed and which consists of three parts: (1) A platform with an expanding metallic ring (Fig. 1); (2) a roentgenographic guide (Fig. 2); and (3) a needle carrier mounted in the protractors (Fig. 3).

TECHNIQUE

First, the platform is attached to the skull by means of inserting the ring into the trephine hole previously made. A complete rigidity is achieved by expanding the metallic ring as much as necessary against the edges of the trephine hole (Fig. 1). Secondly, the roentgenographic guide is at-

Fig. 2. The roentgenographic guide is attached to the platform.

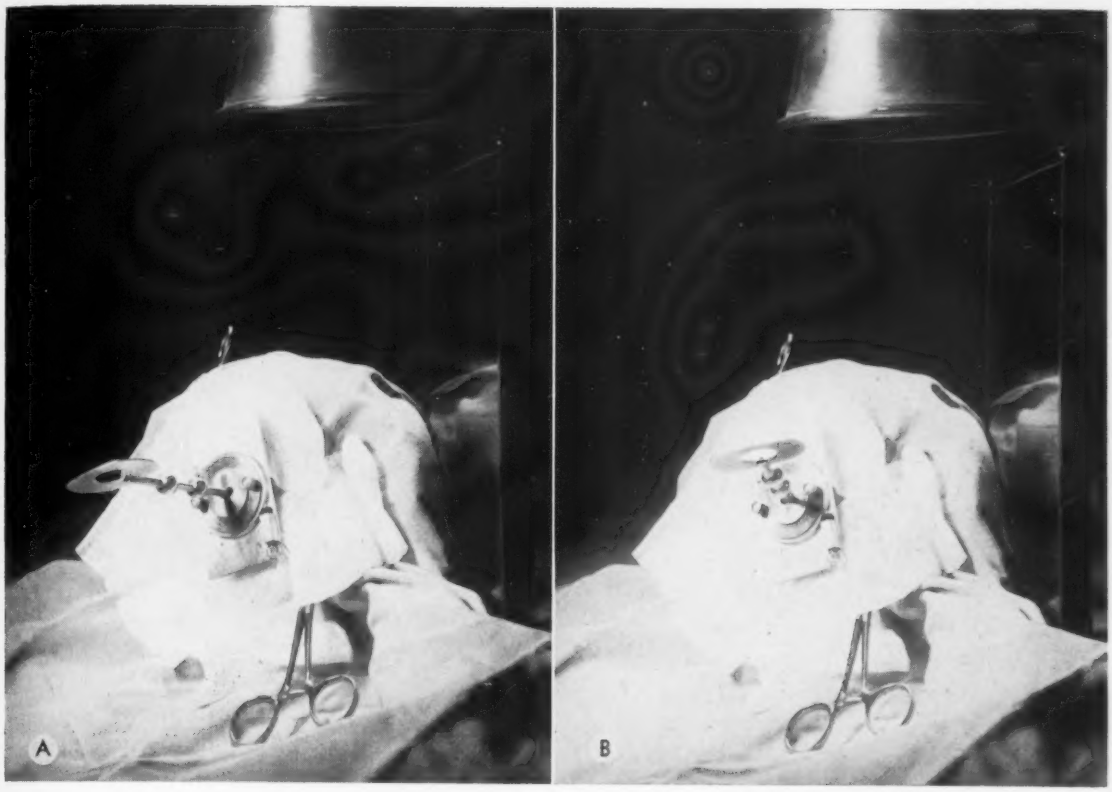


FIG. 4. (*A* and *B*) The stem of the roentgenographic guide is adjusted in the lateral view in such a way that the stem is parallel to the film.

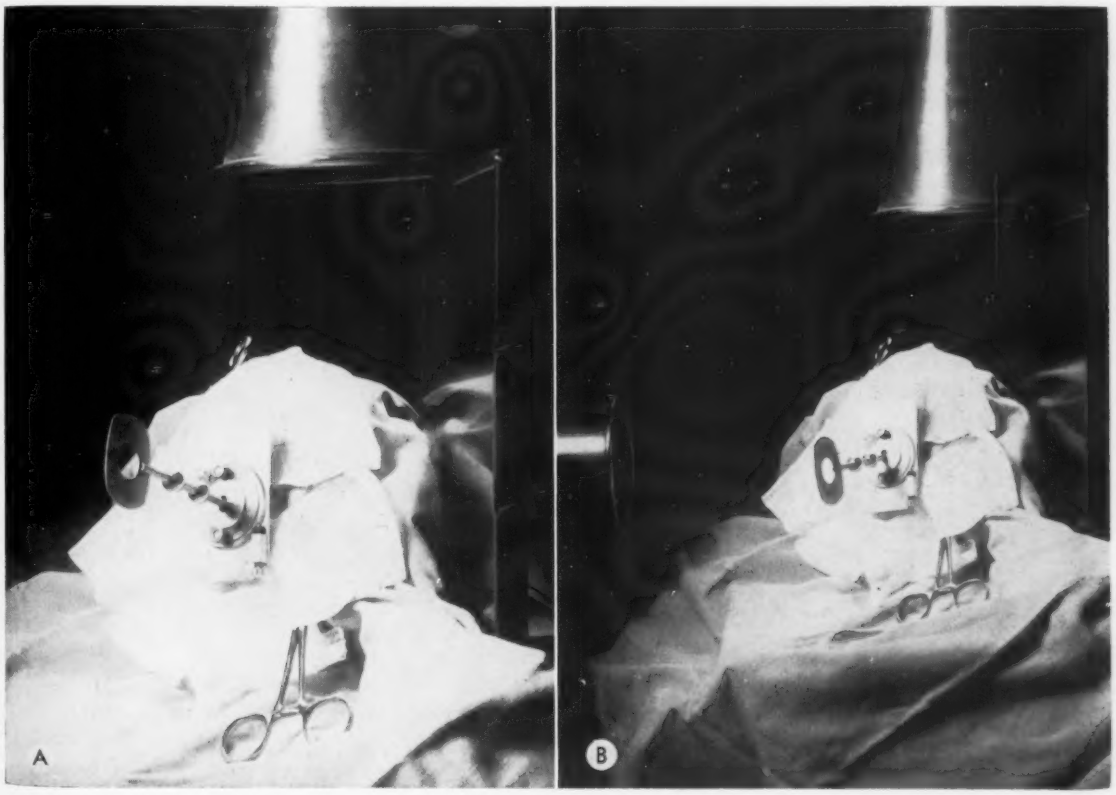


FIG. 5. (*A* and *B*) The stem of the roentgenographic guide is adjusted in the anteroposterior view by placing the stem parallel to the film.

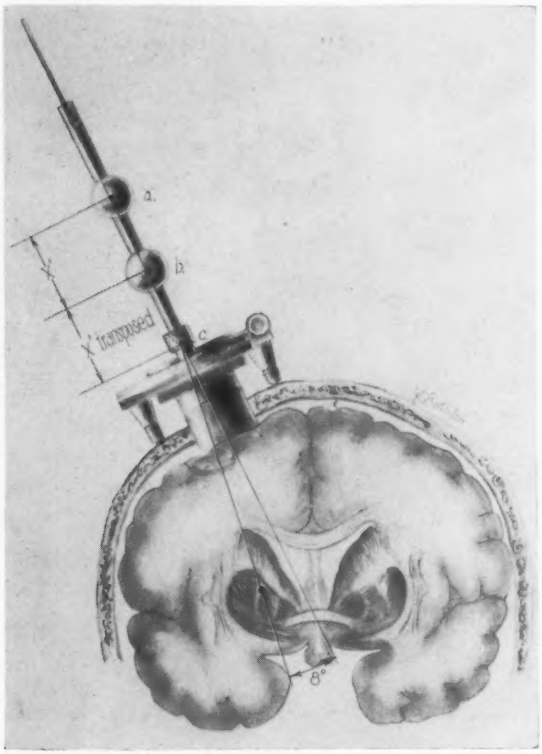


Fig. 6. The zero line is determined by the line connecting the center of the two spheres.

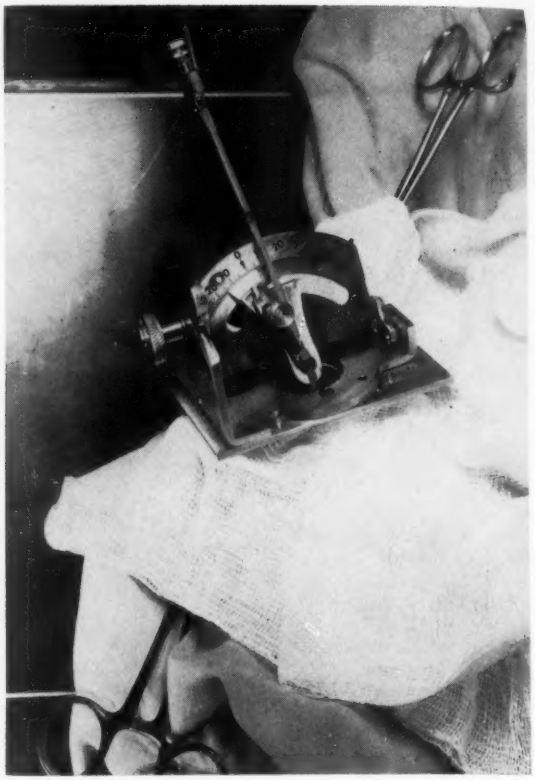
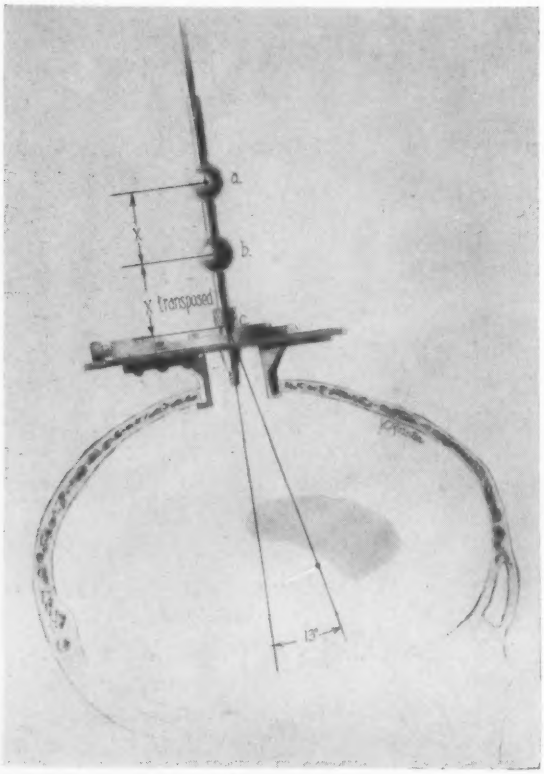


Fig. 8. The needle is introduced fixed in the desired position.



tached to the platform. The stem of this guide is adjusted in such a way that when the anteroposterior and lateral roentgenograms are taken, the stem is parallel in both cases to the film (Fig. 4, *A* and *B*; and 5, *A* and *B*). Thirdly, after taking the roentgenograms and as soon as the film is developed, the zero line and zero point are determined.

As shown in Figure 6 the zero point is determined by marking the distance between the centers of the spheres at c. By tracing a line between the zero point and the target previously selected on the film with the air filled ventricles, we have two angles in the anteroposterior and lateral position (Fig. 6 and 7). A protractor is then

Fig. 7. The zero point is determined by transposing the distance between a and b at c. By tracing a line between the zero point and the target, we have the corresponding angle of 13° in the lateral and 8° in the anteroposterior view.

attached (Fig. 8) with a needle carrier to the platform and by introducing the needle fixed in the desired position, the pre-selected structure is reached. The depth is calculated by deducting the distortion between the actual distance of the center of the two spheres and the same distance marked on the film.

After testing this stereotaxic apparatus in experimental skulls and in cadavers, we have used it in 30 patients with excellent results as far as precision is concerned.

SUMMARY AND CONCLUSIONS

The roentgenologic principles of a new stereotaxic apparatus are formulated. The description of the apparatus is given, emphasizing the importance of the roentgenographic guide which fulfills three functions: (1) Keeps the position of the head in such a way that the zero line is always parallel to the film; (2) the zero line and the zero point are attained by tracing a line connecting and marking the distance of the center of the two spheres; and (3) calculation of the distortion is given by measuring the difference between the actual distance of the center of the two spheres and the same distance measurement on the films.

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THE NORMAL CERVICAL DISKOGRAM

WITH CLINICAL OBSERVATIONS

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THE technique of cervical diskography has been helpfully used by the author since 1952. It was described and reported in 1957.[2,3] Figure 1 shows the approach to the disk space. Once the needle is properly placed in the intervertebral space, approximately .5 ml. to 1 ml. of 70 per cent diodrast is injected. The clinical reaction as regards the production of pain, either radiating, localized or referred, is noted and anteroposterior, posteroanterior and lateral roentgenograms are taken.

The roentgen appearance of the normal cervical intervertebral disk space injected with diodrast has not previously been discussed; however, numerous observations have been made regarding the normal lumbar diskogram.[1]

This report deals with the roentgen appearance of the normal cervical diskogram and certain clinical observations that have been made during the procedure. Conclusions regarding the normal cervical diskogram were somewhat difficult to draw since cervical diskography is performed of necessity only in those individuals of the twenty to seventy year age group who have signs and symptoms of cervical disk disease, usually pointing to rupture or degeneration, and experience showed that it would be unwise to formulate conclusions regarding the normal cervical disk and diskogram from this group of patients. Accordingly, it was necessary to go to a younger age group to look for the normal cervical disks. Inasmuch as these younger individuals had no cervical disk disease which would afford opportunities for cervical diskography, the next most reliable source of "normal cervical disks" in the younger age group seemed to be those who came to autopsy. The cervical disks of such individuals were injected with 70 per cent diodrast immediately after death. Altogether 14 diskographies were performed, the ages ranging between three months and fifty-seven years and the total number of cervical spaces injected amounting to 52.

The normal cervical diskogram has a different appearance from that of the normal lumbar diskogram. In the normal lumbar diskogram (Fig. 2) the centrally injected contrast medium assumes a biloculated shape; one portion surrounds the nucleus pulposus and is contained within the cup-like annulus fibrosus. The contrast medium does not spread posteriorly to the vertebral bodies. Occasionally, it is located centrally within the annulus fibrosus without biloculation, but this occurs in a questionable abnormal disk. The normal cervical disk (Fig. 3) does not exhibit biloculation but the opaque medium remains in the center of the disk as a single collection, without extruding beyond the bodies of the vertebrae. In reviewing the cervical diskograms of the clinically injected cases, some intervertebral spaces were found, the roentgen appearance of which resembled that observed in the cadaver injected intervertebral spaces. Therefore, in subsequent studies an attempt was made to inject the intervertebral space suspected of being diseased and the intervertebral space above and below this level. In a group of over 150 cervical intervertebral spaces injected clinically, there were some intervertebral spaces that fell into the "normal range," using the postmortem injected intervertebral spaces as comparison. It should be stated, however, that in those patients who were examined for suspected cervical disk disease the incidence of multiple, degenerated cervical disks in the injected intervertebral spaces

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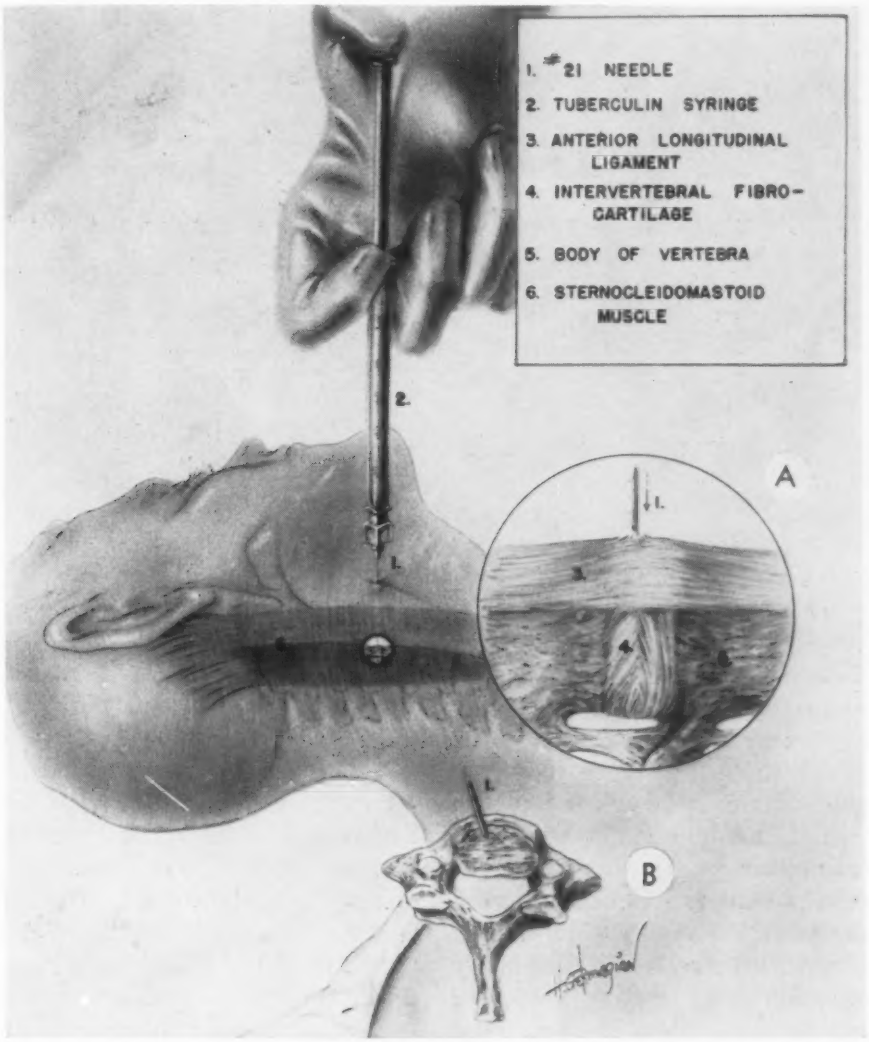

Fig. 1. Position of the head for cervical diskography. Circle insert A shows the needle touching the anterior longitudinal ligament to enter the disk space. The relationship of the needle to the disk space is shown in the lower insert B.

was extremely high and much greater than had been anticipated.

Certain pertinent observation were made at the time of the disk injection. One striking observation was that injection was practically impossible into the normal intervertebral space. This was also borne out by the postmortem studies in the younger individuals. It was with extreme difficulty that these "normal spaces" could be injected with even such small amounts as .1 to .2 ml. of medium. In an effort to evaluate the pressure that is required to inject such "normal intervertebral spaces," a closed air manometer was placed in the circuit to measure the pounds of pressure necessary to drive in .1 or .2 ml. of 70 per cent diodrast. This ranged from 88 to 123 pounds per square inch force. The magnitude of the mechanical force used gives the operator a clue as to whether or not the intervertebral disk space being injected is "normal." If the injection is easily performed with a pressure of less than 40 pounds per square inch, one may conclude that the intervertebral space is not normal. Also, the pain is less when a nonpathologic than when a pathologic intervertebral space is injected.

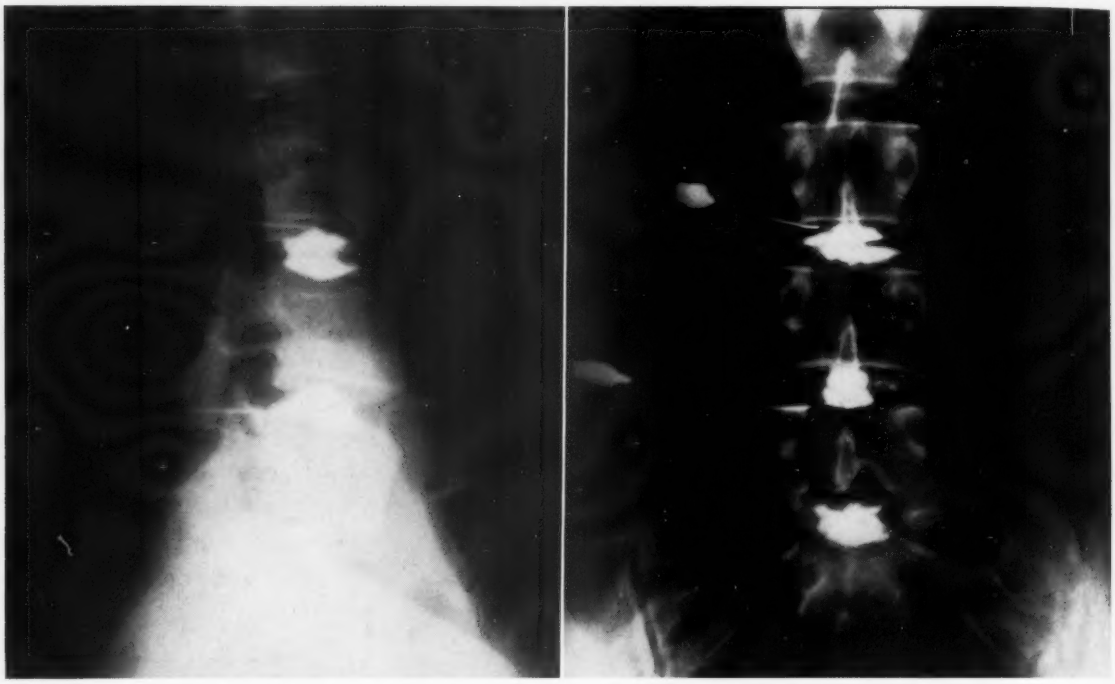

FIG. 2. Lumbar diskograms performed by the posterior-lateral approach. Note the biloculation of the medium centrally.

In inserting the needle it was noted that when the needle made contact with and pierced the anterior longitudinal ligament (Fig. 1*A*), the patient experienced referred suboccipital pain. Introduction of the needle within the intervertebral disk space produced no pain but, when the opaque medium was injected, pain ensued. Posterior cervical pain was experienced to a lesser degree in the "normal disk" cases. Referred pain in the interscapular area did not occur when a normal intervertebral space was being injected; this is in contrast to injection of the degenerated disk space. The higher the space injected, the higher was the location of the referred interscapular pain (approximately 3 cm.). The injected "normal" intervertebral space did not produce radiating pain into the shoulder and arm.

Cervical diskography has the following disadvantages: (1) Information is not obtained regarding the spinal cord or the cerebrospinal fluid bathing the spinal cord. (2) There is a possibility of introducing an infectious process into a relatively avascular area (this has not occurred in this clinic with either cervical or lumbar diskography) although the same can be said for any diagnostic procedure in which the skin is punctured. (3) Since a high percentage of cervical disks shows degeneration, a great number of degenerative intervertebral disks are seen which may not produce spontaneous symptoms and thus may give a false roentgen-positive information.

The advantages of cervical diskography are: (1) Direct information regarding the disk and interspace, the point of pathologic change, is obtained. (2) The contrast medium is quickly absorbed and there is no necessity for its removal. (3) Clinical information is obtained as regards the reproduction of cervical, suboccipital, radiating and referred pain on injection of the abnormal intervertebral space. (4) Information can be obtained about the point of rupture of the annulus fibrosus and the direction of the extrusion (Fig. 4). (5) Definitive information can be obtained about the more laterally

herniated disks and the minimal midline herniations which fail to distort the dural sac. (6) There is no puncture of the meninges or possible bloody contamination of the spinal fluid and there is no disturbance of the dynamics of the spinal fluid which in the occasional case might worsen the symptoms. (7) The procedure can be employed on an out-patient basis. (8) Fluoroscopy and extensive radiation exposure is not required. (9) With moderate experience the examination can be accomplished quickly (fifteen to twenty minutes). (10) The morbidity and pain that the patient suffers is short in duration, lasting approximately one to two minutes for each intervertebral space injected and this distress of the patient can be used to good advantage clinically, since it is often a precise reduplication of the type of pain which caused the patient to seek medical attention. (11) This technique also permits the injection of a colored dye such as methylene blue into the disk space at the appropriate disease level to assist localization when subsequent surgery is desired.

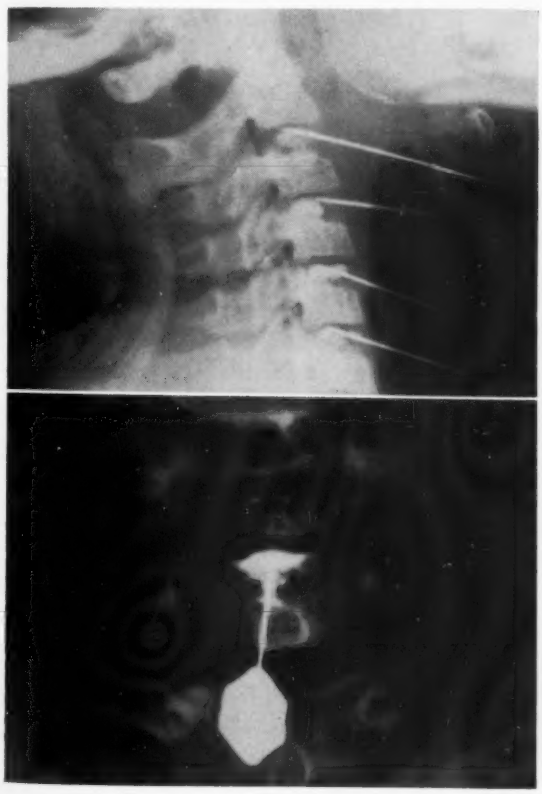

Fig. 3. Normal cervical diskograms obtained on young postmortem cases. Note the centrally located single area of diodrast.

Fig. 4. Anteroposterior cervical diskogram showing lateral extrusion of contrast medium along the joint of Luschka and the neuroforamina at the third to fourth interspace. Surgical intervention confirmed the rupture with relief of symptoms.

CONCLUSIONS

If the differential diagnosis is obscure and intraspinal canal disease is suspected, cervical diskography should not be employed. The procedure is more fruitful for the proper localization of the diseased intervertebral space producing cervical shoulder, arm, and hand pain.

SUMMARY

The normal cervical diskogram differs from the normal lumbar diskogram. Relatively few normal cervical diskograms are obtained in individuals who have passed the age of twenty-five or thirty years. The

"normal intervertebral disk" is difficult to inject and will allow the injection of only a small amount of contrast medium. Posterior cervical pain is produced by increasing the intervertebral space mass with the injected material; this may be the result of mechanically stretching the longitudinal ligaments. The reproduced cervical shoulder, arm, and hand pain is useful for clinical evaluation. There is no other morbidity. The advantages of cervical diskography are greater than the disadvantages. The referred interscapular pain can be reproduced and has a topographic reference to the cervical space level. Suboccipital referred pain can be reproduced by mechanical stimulation of the anterior longitudinal ligament.

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BLOCK OF THE SPINAL CANAL CAUSED BY HERNIATED DISK*

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IN MYELOGRAPHY, with the demonstration of incomplete or complete block to the passage of the contrast material, the diagnosis of a tumor is generally given early and paramount consideration. Other causes of block such as adhesive arachnoiditis, spinal cord varices, syringomyelia, tuberculosis, fracture-dislocations and tumor-like swellings of the spinal cord in infectious or toxic myelitis are seen with varying degrees of frequency. Although a herniated nucleus pulposus is sometimes considered a causative factor for incomplete block, the frequency of such an occurrence and the characteristic features that may enable such a diagnosis to be made are not sufficiently appreciated. It is the purpose of this paper to present 13 cases of herniated nucleus pulposus in the cervical and lumbar regions, which on myelography demonstrated features of block, usually simulating a tumor.

The fact that a herniated disk may cause a spinal block was realized nearly thirty years ago. Dandy,[1] in 1929, reported 2 cases in which the spinal canal was completely blocked in the midlumbar region and a preoperative diagnosis of tumor of the cauda equina or carcinoma of the vertebra was made. In both instances, a loose cartilage segment from an intervertebral disk, which Dandy has described as a fragment of disk becoming detached and bulging posteriorly into the spinal canal, was found at operation.

Love,[6] in 1944, discussed the differential diagnosis of intraspinal tumors and protruded intervertebral disks together with their surgical treatment. He emphasized the high protein value of the spinal fluid in tumors, as against the normal protein level in protruded intervertebral disks, but omitted any discussion of the differential roentgen findings.

Other articles by Peyton and Simmons,[8] Kennedy *et al.*,[5] Kaplan and Umansky,[4] Paterson and Gray,[7] Grantham and Spurling,[3] and Uiberall *et al.*[10] have appeared in the literature in the intervening years, up through 1957. None of these authors have made more than passing reference to the roentgenographic features of block caused by a herniated nucleus pulposus.

Two classic articles, one by Epstein[2] in 1949 and the other by Tucker[9] in 1956, have ably dealt with this subject. Epstein found a complete block due to herniated nucleus pulposus in 5 out of 150 lumbar myelograms, with the disks generally being seen in the midline at operation. He reported that myelograms demonstrated irregular dentate serrations at the end of the contrast column when the medium was instilled from above, and pointed out that the column was more irregular at the site of block when the opaque medium was instilled from below. Epstein stated that there was usually a pronounced neurologic syndrome, often indistinguishable clinically from that of a cauda equina tumor. Tucker found 75 instances of complete block in 196 consecutive myelographies, for a rather startlingly high percentage of 38.8. Of these blocks, 2 in the cervical region and 10 in the lumbar area were due to herniated nucleus pulposus. Tucker did not attempt to differentiate the appearance of these blocks roentgenographically from those caused by tumors and other etiologic factors.

CLINICAL MATERIAL

We have collected 13 cases of herniated

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nucleus pulposus or intervertebral disk protrusion causing block of the spinal canal in varying degree, as manifested in the myelogram. These cases have been compiled from the files over the past ten years at Montefiore Hospital, with no attempt made to gather statistics as to the percentage of block cases in relationship to the total number of myelographies performed during this period.

Of these 13 cases, 10 were males and 3 were females. The age incidence varied from twenty-eight years to seventy-three years, with involvement in the fourth and fifth decades being most common. All patients were white (our hospital population is predominantly white). Table 1 lists the age, sex, pertinent clinical symptoms and neurologic abnormalities, the preliminary roentgen findings and the myelographic findings. The degree of block is indicated in the myelographic findings. The data relating to the spinal fluid, particularly the protein determination, spinal fluid pressure, and manometrics are also included where available. The operative findings are noted briefly in each case.

In 5 cases, the block was complete, in 4 cases almost complete and in 4 cases it was incomplete. In 3 cases the herniated nucleus pulposus causing the block was present in the cervical spine: in 1 occurring at the C_4–C_5 interspace and in 2 at the C_5–C_6 interspace. None was seen in the thoracic spine. In the remaining 10 cases, a herniated disk was found in the lumbar spine: five times at L_4–L_5, twice at L_5–S_1 and one time each at the L_1–L_2, L_2–L_3 and L_3–L_4 interspaces. The clinical symptoms and physical findings were not sufficiently characteristic to suggest the possibility of a block, complete or incomplete. In 3 instances, the spinal fluid findings were not available to us. In the remaining 10 cases, the total protein was considerably elevated in 3 instances, 162 mg. per cent, 166 mg. per cent and 184 mg. per cent, respectively. In this connection Love states that a total protein value of over 100 mg. per cent generally differentiates a tumor from a protruding disk in the case of block, with the high protein level indicating a tumor. This observation was not substantiated in the 3 cases just mentioned (Cases 5, 7 and 8).

FIG. 1 Case 1. Pantopaque instilled from above outlines a complete block at C_4–C_5, suggesting an intramedullary tumor. Intervertebral disk protrusion found at operation.

ROENTGEN FINDINGS

The findings on the preliminary roentgenograms were not significantly different from other instances of herniated nucleus pulposus. Usually the changes consisted of thinning of the disk cartilage at the site of disk protrusion, with secondary exostosis formation and reactive osteosis.

MYELOGRAPHY

Characteristic examples of complete and incomplete blocks of the pantopaque column due to herniated disk are shown in Figures

1 through 13. Figures 1 through 3 (Cases 1, 3 and 5) demonstrate herniated disks in the cervical area with complete blocks. An intramedullary tumor is simulated in Figures 1 and 3. Figures 4 through 10 show herniated disks causing complete blocks in the lumbar spine (Cases 6, 7, 8 and 9). Figures 11 through 13 are examples of incomplete block with large centric defects (Cases 12 and 13). In the cases of incomplete or almost complete block, a trickle of opaque medium passed either cephalad or caudad, depending on the site of instillation of the pantopaque and on the location of the herniated nucleus. A serrated margin at

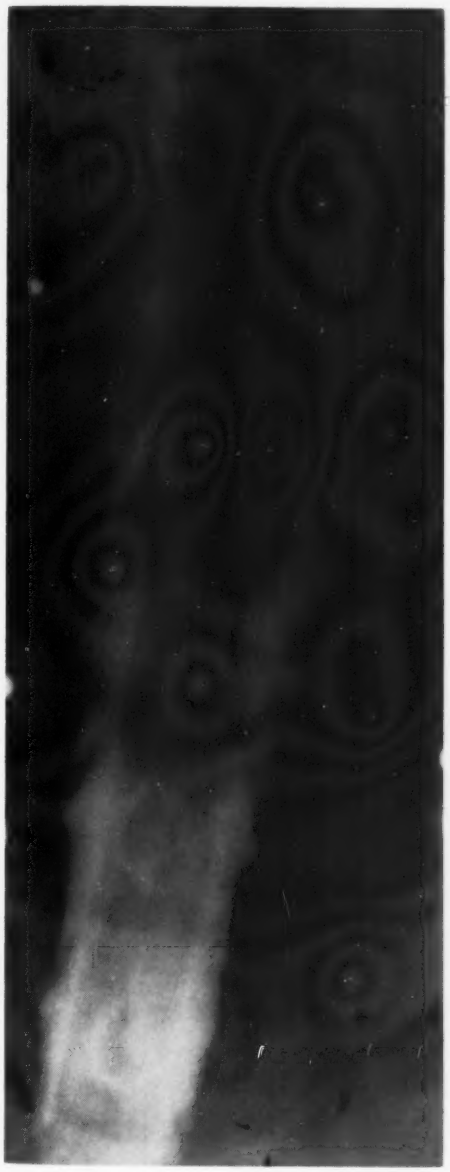


Fig. 2. Case 3. Pantopaque instilled from below outlines almost complete block at C5–C6. Herniated disk protrusion found.

Fig. 3. Case 4. With pantopaque instilled from above, a block is shown at a point just below the L3–L4 disk space. The protruding herniated nucleus was found operatively at L4–L5. Note the irregular serrated margin at the lower surface of the pantopaque column.

TABLE I

TABULAR SUMMARY OF DATA ON 13 CASES

Case	Age	Sex	Related Symptoms	Pertinent Neurologic Abnormalities	Findings on Preliminary Roentgenograms	Myelographic Findings	Pertinent Spinal Fluid Findings	Operative Findings
1 S.K.	40	M	Pain in neck. Weakness in extremities	Spastic shuffling gait. Weakness of right hand and lower extremities. Positive Hoffmann's sign bilaterally. Absent abdominal reflexes. Increased knee and ankle jerks	No preliminary roentgenograms available	Complete block at level of C_4–C_5, suggesting intramedullary tumor. Myelography done via cisternal puncture (Fig. 1)	Not available	Midline herniation of nucleus pulposus at C_4–C_5 with cord compression
2 E.W.	73	F	Weakness and pain in both lower extremities	Absent abdominal reflexes. Absent knee and ankle jerks bilaterally	Spondylosis deformans and degenerative disk disease, particularly at L_5–S_1	Almost complete block at L_2–L_3	Protein—24 mg.%	Markedly swollen nerve root. Dense adhesions of connecting nerve root, dura, posterior spinous ligamentum flavum at L_2–L_3. Calcified disk with ectopic focus disk cartilage. Also herniated disk at L_3–L_4
3 H.S.	59	M	Weakness of right hand and leg. Numbness about buttocks	Weakness of right upper and lower extremities. Impaired position sense of right hand	Spondylosis deformans, with thinning of disk cartilage at C_5–C_6	Incomplete block at C_5–C_6 with concave upper border of contrast medium (Fig. 2)	Protein—72 mg.% Pressure—normal Manometrics—normal	Calcified protruding disk at C_5–C_6
4 A.P.	39	M	Low back pain radiating down sciatic aspect of left lower extremity into toes	Bilateral paravertebral spasm. Bilateral Lasègue's sign. Diminished right knee jerk. Absent ankle jerks	Spondylosis deformans with narrowing of disk cartilage at L_5–S_1	Complete block to caudad flow of pantopaque 2.5 cm. above L_4 disk site with serrated lower margin (Fig. 3)	Not available	Herniated intervertebral disk in midline at L_4–L_5
5 I.K.	46	M	Pain in left thigh, calf and foot. Thermal anesthesia, left lower trunk	Sensory level at T8–T9. Brown-Séquard type picture. Bilateral Babinski sign	Postural changes of cervical spine with spondylosis deformans and degenerative disk disease at C_5–C_6	Almost complete block at C_6–C_7 (2.3 cm. from C_5–C_6 disk space) with concave defect, suggesting spinal cord tumor (Fig. 4)	Protein—166 mg.%	Herniated midline disk at C_5–C_6
6 F.B.	37	M	Low back pain radiating down left thigh	Diminished sensation of outer aspect of left leg and foot. Bilateral foot drop	Degenerative disk disease at L_4–L_5 with minimal thinning at L_3–L_4	Complete block at L_3–L_4. Serrated appearance at block margin (Fig. 5)	Protein—69 mg.% Pressure—normal Manometrics—normal	Herniated midline disk at L_3–L_4. Left-sided herniated disk at L_4–L_5

TABLE I—*continued*

Case	Age	Sex	Related Symptoms	Pertinent Neurologic Abnormalities	Findings on Preliminary Roentgenograms	Myelographic Findings	Pertinent Spinal Fuid Findings	Operative Findings
7 M.S.	34	M	Low back pain with inability to void	Loss of sensation in perineum and lower extremities. Lasègue's sign on right. Loss of right ankle jerk	Thinning of disk cartilages at L5–S1 and L4–L5	Complete block above L5–S1 disk site. Serrated appearance at inferior margin (Fig. 6 and 7)	Protein—184 mg.% Pressure—normal Manometrics—normal	Massive disk, herniated centrally at L5–S1, lying free in spinal canal
8 D.B.	44	F	Low back pain radiating down posterior aspect of left leg	Diminished left ankle jerk. Limitation of straight leg raising. Diminished sensation over left leg	Rotary scoliosis and spondylosis deformans of lumbar spine	Almost complete block to cephalad flow below L1–L2, with hour-glass defects at L4–L5 and L2–L3. Serrated edges of upper margin of pantopaque column (Fig. 8, *A* and *B*)	Protein—162 mg.% 214 mg.% Pressure and manometrics not recorded	Herniated disk at L1–L2 in central position, but more prominent on left. L2–L3 and L4–L5 not explored
9 A.S.	28	F	Low back pain and pain in left thigh and leg	Positive Lasègue's sign on left	Preliminary roentgenograms not available	Complete block 2 cm. above L5–S1 with caudad flow. Serrated inferior margin (Fig. 9 and 10)	Protein—31 mg.% Manometrics not recorded	Large herniated disk at L5–S1
10 H.T.	59	M	Pain left side of back, hip and left leg	Absence of left ankle jerk	Thinning of disk cartilage at L3–L4 and L5–S1	Large filling defect at level of L4, simulating neoplasm with incomplete block	Protein—56 mg.%	Large disk lying free in extradural space, L5–S1
11 H.A.	56	M	Low back pain radiating down posterolateral aspect of left thigh and leg	Left knee jerk more active than right. Ankle jerk on right more active than left. No sensory changes	Moderate generalized spondylosis deformans	Complete block at L4–L5 with serrated margin	Protein—45 mg.% Manometrics not recorded	Large midline herniated disk at L4–L5
12 K.D.	43	M	Low back pain	Weakness in right lower extremity with absent ankle jerk. Hyperalgesia of right lower extremity	No significant findings	Incomplete block at L4–L5 with serrated margin (Fig. 11 and 12)	Not available	Herniated disk at L4–L5, mostly midline
13 S.Y.	51	M	Intermittent low back pain radiating into left leg	Left foot drop with atrophy of outer tibial muscles. Absent left ankle jerk. Absent cremasteric reflex	Thinning of disk cartilage at L4–L5 with loss of lumbar lordosis	Incomplete block at L4–L5 (Fig. 13)	Protein 92 mg.% Pressure and manometrics not recorded	Extruded midline disk at L4–L5

FIG. 4. Case 5. Pantopaque instilled from below delineates what appears to be a block at C6–C7, suggesting an intramedullary tumor. Actually, the herniated nucleus was found at C5–C6. This is an example of a case in which the actual disk was several centimeters removed from the site of the myelographic block.

either the superior or inferior aspect of the pantopaque-filled canal could be seen (again depending on the direction of the flow) at the site of block. In cases of incomplete or almost complete block, the finding of an indentation on the anterior aspect of the pantopaque column on the lateral decubitus roentgenogram was helpful (Fig. 12). A large gap defect (Fig. 11 and 13) was noted, at times, between the serrated pantopaque

FIG. 5. Case 6. Pantopaque moving caudally is blocked at L3–L4 because of the herniated disk. The inferior serrated margin is clearly defined.

margin and the rest of the opaque medium which had trickled past the site of obstruction. In 4 cases (Cases 1, 4, 5 and 9) the block was situated, respectively, 2.5, 2.5, 2.3 and 2.0 cm. removed from the disk site, as seen on the myelogram (Fig. 1, 3, 4 and 10). The reason for this finding is not clear but associated edema (cauda equina in the lower lumbar area and spinal cord in the cervical region) could be responsible, with migration of disk material also possible.

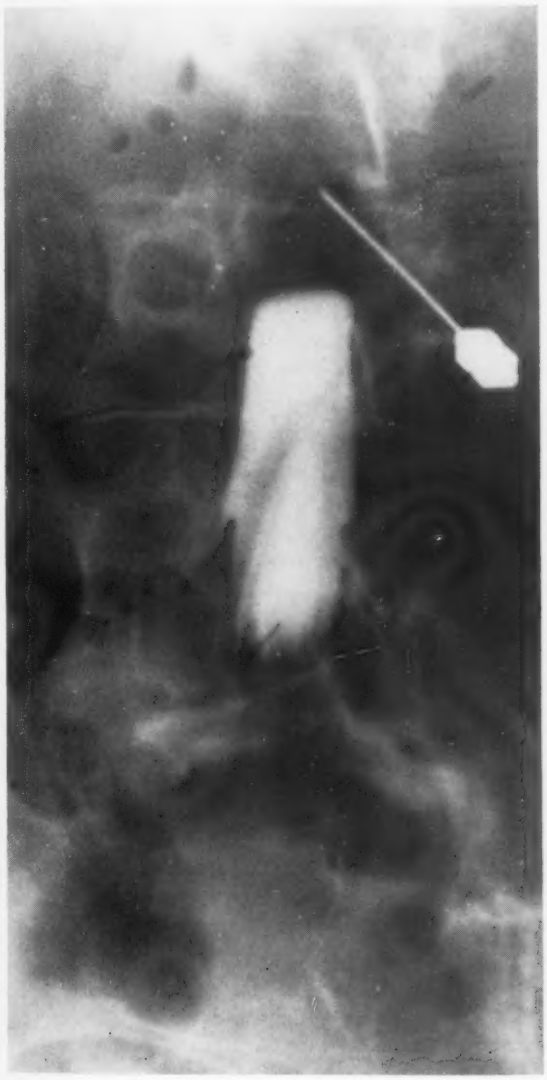


Fig. 6. Case 7. Pantopaque instilled from above is blocked well above the L5–S1 disk site. The herniated nucleus was found at L5–S1 at operation. The serrated inferior margin of the pantopaque column is clearly outlined.

Fig. 7. Case 7. Lateral decubitus view of case in Figure 6.

A tumor was simulated or considered in practically all of our 13 cases; however, a neoplastic resemblance was most marked in instances of complete or almost complete block (Cases 1, 2, 4, 5, 6, 7, 8, 9 and 11).

DISCUSSION

Although intervertebral disk protrusion is not the most common cause of spinal block (12 out of 75 cases in Tucker's series and 5 out of 150 cases in Epstein's series), this entity occurs often enough for the radiologist and neurosurgeon to be alerted to its possibility. The diagnosis of a tumor is frequently entertained by the clinician and sometimes appears to be corroborated on the myelogram. Clinically, the diagnosis of a herniated disk should be considered in a case of complete or incomplete block (by myelography) when such block is demonstrated in a male patient in the lumbar region (or cervical area) with neurologic deficits usually localized to a small segment and with a slight to moderate elevation of the spinal fluid protein. In instances of an elevated spinal fluid protein and evidence of block on manometric study and on myelography, the differential diagnosis is not always easy. However, there are certain features that may indicate the correct answer. A serrated upper or lower border of the pantopaque column on myelography in a case of complete block (depending on the direction of flow) points to a herniated disk, particularly in the lower lumbar or lower

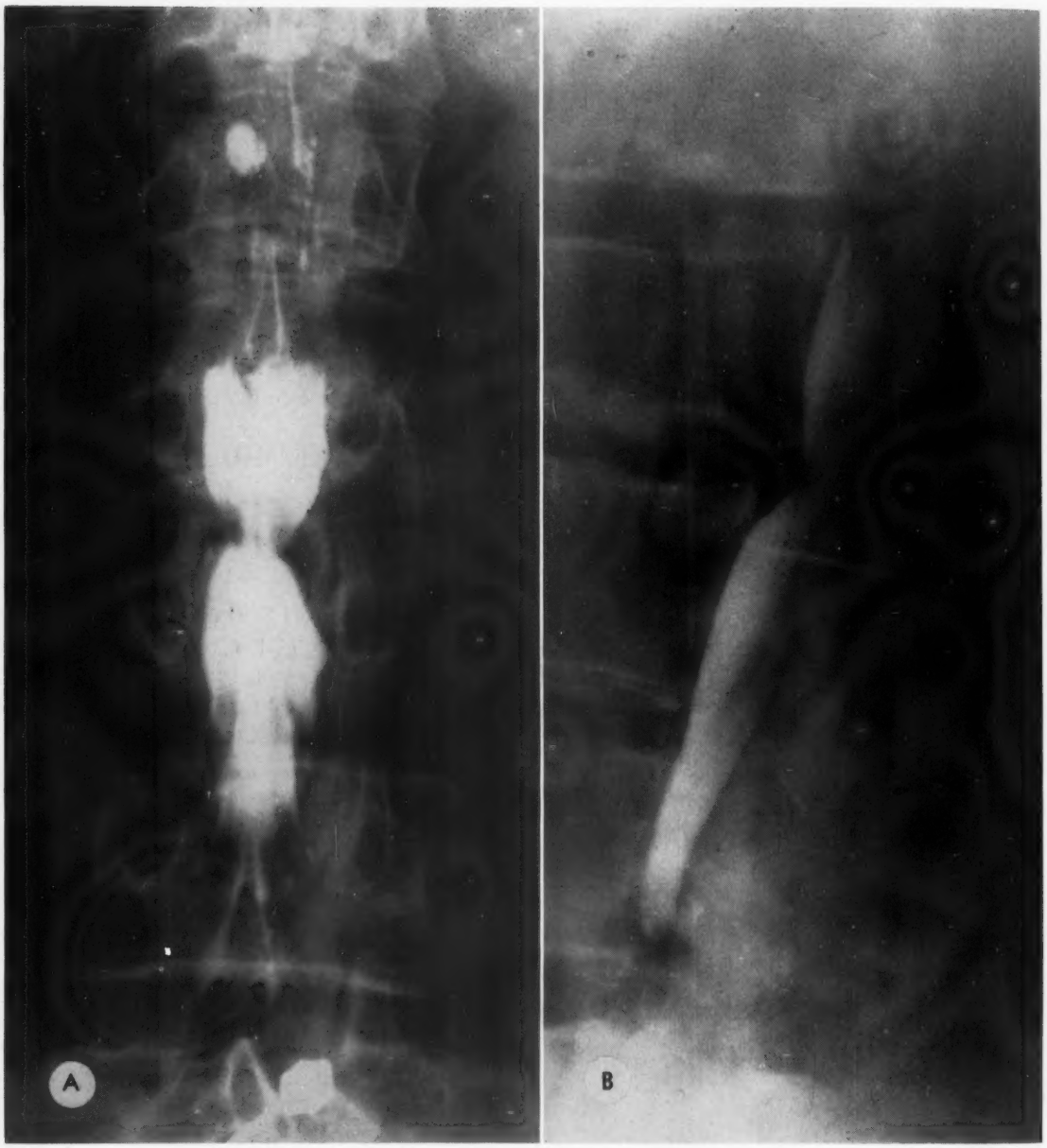


FIG. 8. Case 8. (*A*) Pantopaque instilled from below is blocked 2 cm. below the L1–L2 disk site. The herniated disk was found at L1–L2. An hour-glass defect at L2–L3 could be another herniated nucleus, but this site was not operatively explored. Upper serrated border clearly seen. (*B*) Lateral plane. Upper serrated border clearly outlined. L4–L5 also not explored Gap defects are seen in lateral view.

Fig. 11. Case 12. With pantopaque instilled from above, a large gap defect is noted at L4–L5, giving the appearance of an incomplete block. A serrated inferior margin is noted at the L4–L5 site. A herniated disk was found at L4–L5. ⟶

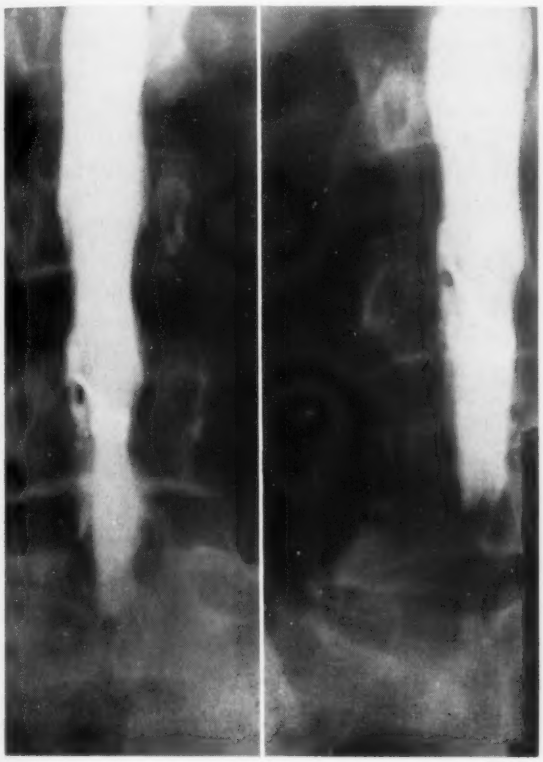
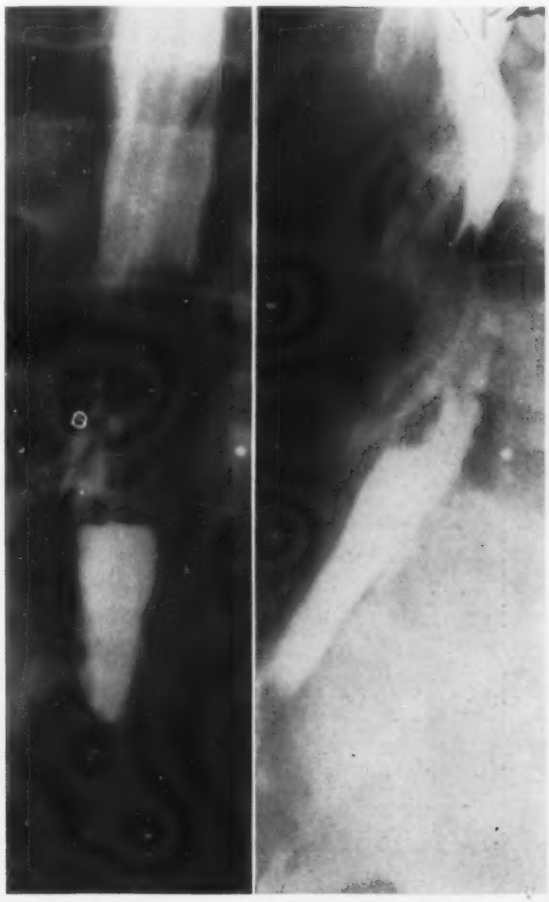


Fig. 9. Case 9. Obstruction to pantopaque column after instillation from above is seen just below the L4–L5 disk site. The herniated disk was found at L5–S1 at operation. The serrated inferior margin is well outlined.

Fig. 10. Case 9. Lateral decubitus view of case in Figure 9, similarly showing the block well above the site of the herniated nucleus with the serrated lower margin.



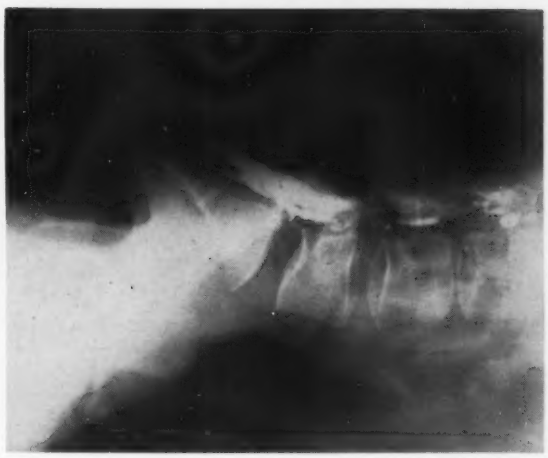


Fig. 12. Case 12. A lateral decubitus view of case in Figure 11. Pantopaque coursing upward from below outlines the site of incomplete block just below L4–L5 with a protrusion on the anterior aspect of the pantopaque column just below the site of the herniated disk. This is a characteristic finding in the lateral decubitus roentgenogram.

FIG. 13. Case 13. The pantopaque instilled from above is incompletely blocked at L4–L5 with a serrated lower margin. A protruding disk was found at L4–L5. The large gap defect again simulates a cauda equina tumor. An hour-glass deformity at L3–L4 with disk cartilage thinning at this site may be due to a second herniated nucleus but this area was not explored.

cervical region. In the case of an incomplete block in one of these areas, an anterior defect of the oil column in the lateral decubitus view at the site of block should suggest a protruding disk.

SUMMARY AND CONCLUSION

Thirteen cases of complete, almost complete or incomplete block caused by intervertebral disk protrusion are presented. A summary of the age, sex, symptoms, neurologic abnormalities, preliminary roentgen findings, myelographic findings, spinal fluid determinations and operative results is given in tabular form.

The characteristic features of a herniated disk, which blocks the spinal canal and simulates a tumor, are stressed.

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EXTENSIVE LUMBAR MENINGOCELE ASSOCIATED WITH NEUROFIBROMATOSIS*

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THE first case of intrathoracic meningocele associated with neurofibromatosis was described by Pohl[15] in 1933. Twenty-eight cases of this abnormality were reported subsequently, but none was observed in the lumbar spine and primarily intravertebral in location. This case of lumbar meningocele associated with neurofibromatosis supports the concept that meningoceles are embryologic mesenchymal defects.

REPORT OF A CASE

R. E. C., a twenty-seven year old Caucasian male sailor, was admitted to the St. Albans Naval Hospital on February 1, 1958, complaining of low back pain of ten days' duration. He did not remember any previous episodes of lumbosacral pain and as a boatswain's mate had performed strenuous physical tasks for the past six years. There was no history of any familial disease. Four siblings were living and well. Physical examination revealed numerous fine cutaneous nodules and small pigmented areas. Several 1 to 2 cm. soft nodules (molluscum fibrosum) were noted on the trunk and forehead (Fig. 1). The neurologic examination was within normal limits as was the remainder of the physical examination. Hemogram, urinalysis, and spinal fluid chemistries and pressures were normal. Roentgenograms (Fig. 2 and 3) of the lumbosacral spine revealed deep scalloping of the posterior portion of the vertebral bodies of T-10 through L-4 and marked thinning of the pedicles throughout this area. A diagnosis of lumbar meningocele was made. Pantopaque myelography (Fig. 4) confirmed the diagnosis. Several small meningocele sacs were demonstrated protruding through the intervertebral foramina. An intravenous pyelogram revealed lateral displacement and scalloping of the right ureter below the renal pelvis (Fig. 5). The right ureter near the pelvic brim was displaced medially and small bowel studies also suggested a mass in this region (Fig. 6). These defects probably represented neurofibromatous masses. A barium enema examination was negative. After extensive consultation the neurosurgical group decided against surgery at this time since the patient was now asymptomatic. A back brace was ordered.

Comment. Potential hazards consist of (1) possible further compression fracture of the weakened vertebra, (2) enlargement and rupture of the meningoceles with sudden decrease in intraspinal pressure, late infection and meningitis, (3) herniation of the meninges into the retroperitoneal space

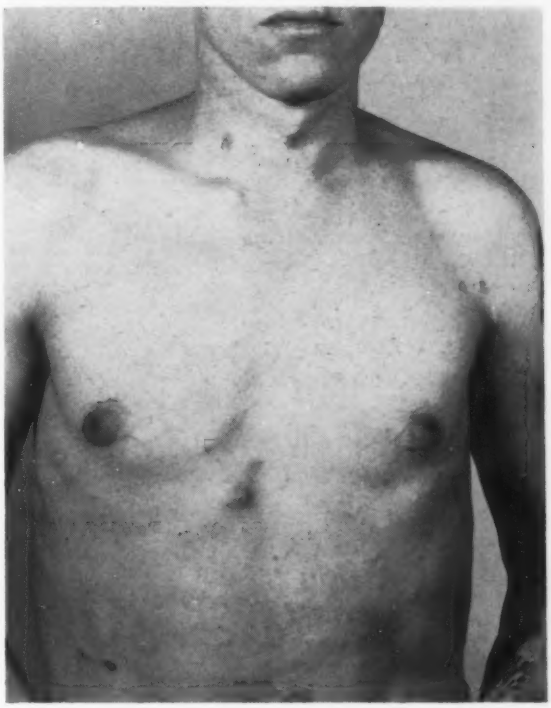

FIG. 1. The entire body is covered with fine cutaneous nodules and café au lait spots. Note the 1 cm. in diameter soft nodule adjacent to the xiphoid.

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FIG. 2. Anteroposterior roentgenogram of the lumbosacral spine reveals severely eroded pedicles of the lower thoracic and upper lumbar regions. There is a minimal compression fracture of the body of L-2.

FIG. 3. Lateral roentgenogram of the lower thoracic and lumbar spine demonstrates deep concave erosions of the vertebral bodies with very little effect on the resilient intervertebral disk. Partial collapse and anterior displacement of the second lumbar vertebral body have occurred.

resulting in pressure symptoms, and (4) sarcomatous change to which deep and visceral neurofibromas are prone; this has been a frequent cause of death in von Recklinghausen's disease.[1]

DISCUSSION

The normal development of the spinal cord occurs from neural, mesodermal, and

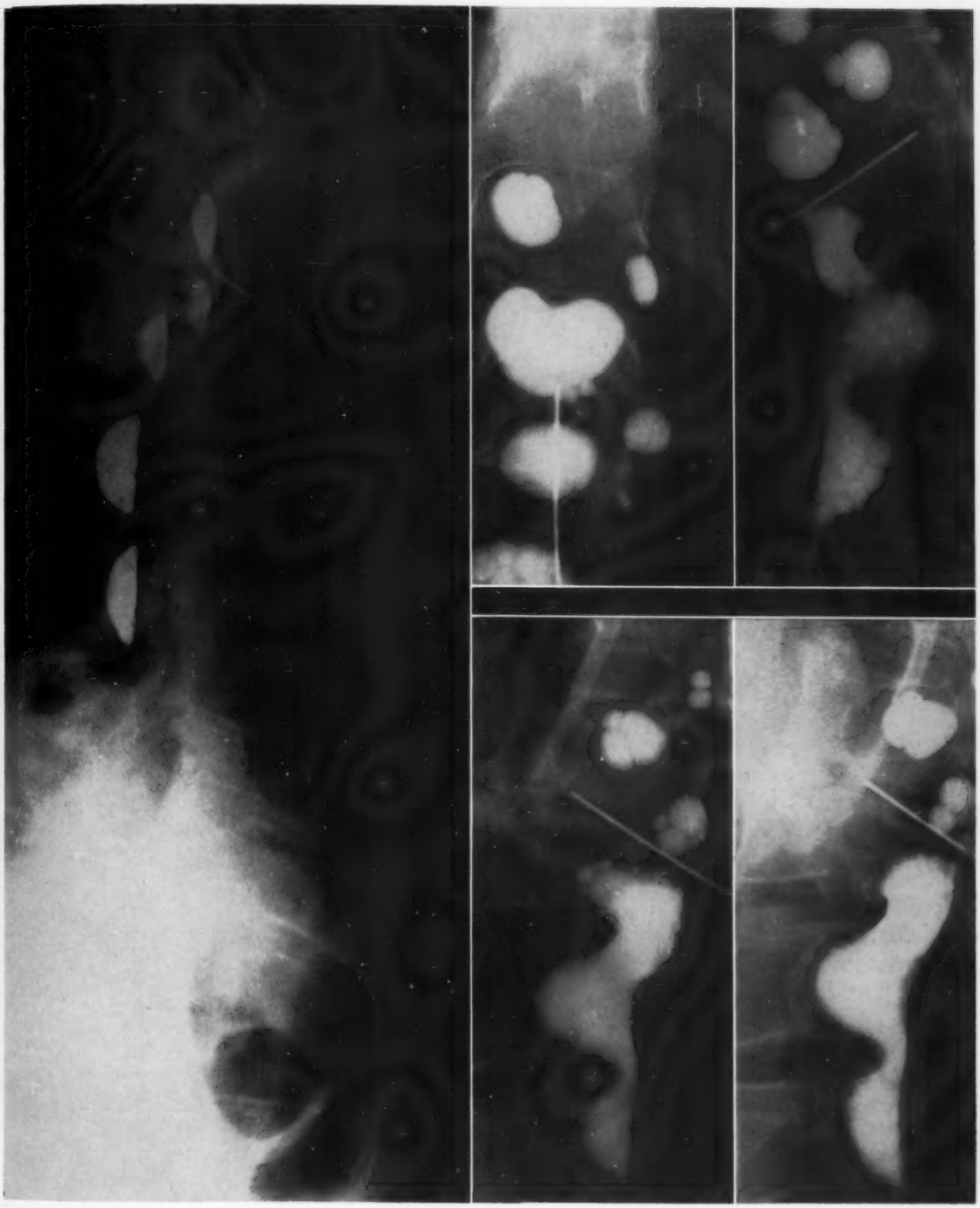

Fig. 4. Myelograms demonstrate herniation of the meninges outside the confines of the vertebral canal. The horizontal lateral myelogram shows the concavities of the vertebrae to be occupied by pantopaque filled meninges.

cutaneous derivatives of the embryonal tissues in the dorsal median region of the embryo. This consists of the closure of the ectodermal neural tube during the third week of embryonic life and closure of the first cervical to fourth sacral vertebral arches during the eleventh week. The meninges, vertebral arches, and sheaths of

FIG. 5. An intravenous pyelogram discloses scalloping in the upper third of the right ureter probably due to retroperitoneal neurofibromata.

peripheral nerves arise from the mesenchyme.

Keiller[8] has divided closure defects into (1) gross mesoblastic, (2) primarily mesoblastic but having an ectodermal component, and (3) primarily ectodermal with contributing mesodermal defects. Lichtenstein[11] prepared a similar classification listing a mesodermal embryologic origin for dural defects. The etiology of these defects occurring in early intrauterine life is unknown, but the occurrence of meningocele with neurofibromatosis is of importance. Neurofibromas and neurofibromatosis are known to arise from the connective tissues of the perineurium (mesenchymal).

There are three basic groups of defects: (1) The most benign, the meningocele, represents a mesodermal defect affecting primarily the dura which then herniates with the arachnoid membrane through intervertebral foramina or bony defects. There may be no herniation of the apparently normal meninges in mesodermal defects affecting only the vertebral body or neural arch (spina bifida occulta). (2) With complete closure of the neural tube, except for a small area which is adherent to a portion of the sac, a meningomyelocele results. This defect is primarily ectodermal accompanied by secondary mesodermal abnormalities. (3) The most serious developmental defect is complete rachischisis (araphia) resulting from failure of closure of the neural tube with the imperfect cord lying exposed on the back of the newborn.

Several explanations of the vertebral deformities associated with meningoceles have been advanced: (1) periosteal neurofibromas[15] (only excess osteoid tissue has been found on microscopic section of verte-

FIG. 6. Small bowel study shows a persistent extrinsic pressure defect on the ileum. This probably is due to visceral neurofibromata.

brae),[6] (2) imbalance of the autonomic nervous system producing endarteritis in the abnormal vertebrae,[13] (3) primary dural defects,[2,3,4,7] and (4) multiple congenital mesodermal anomalies.[10,12,14] That the basic defect is weakness of the meninges, especially the dura, is supported by the following observations: (1) Many intrathoracic meningoceles are associated with another mesenchymal defect, neurofibromatosis, and (2) they produce an effect on the vertebral column resembling that of aortic aneurysm. In both aneurysms and meningoceles the abnormal vessel wall or meninges allow the normal pulsations to erode the hard vertebral body, sparing the resilient intervertebral disk. The marked fluctuations in spinal fluid pressure are well known.

The familial trend was demonstrated when a questionnaire[17] revealed fifty-six times the incidence of the general population for families in which a meningocele, myelomeningocele or encephalocele had already occurred. It was also noted that the incidence of any deformity in families with these malformations was thirty-seven times the incidence of the general population. The usual incidence of meningocele, myelomeningocele, and encephalocele is about 1 in 1,000 births. Three quarters of these are myelomeningoceles. Females outnumber males 1.6 to 1 and 20–30 per cent of all patients are unhampered by their anomaly.

SUMMARY

The first case of a lumbar meningocele associated with neurofibromatosis is reported. A mesodermal origin for this combination has been suggested by the occurrence of thoracic meningoceles with neurofibromatosis. This case further supports the concept of a lack of specificity for the thoracic spine.

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X-IRRADIATION EXENCEPHALY*

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TERATOLOGIES (congenital anomalies) can be produced only by insult of the developing embryo or fetus at certain critical stages, prior to the development of the organs concerned. Anomalies of every organ system may occur, such as of the brain, skeleton, circulation, heart, kidneys, muscles, etc., and they may be caused by a variety of agents injected into the pregnant animal (see discussion) or by penetrating ionizing radiations. Some of these chemical agents have been designated as "radiomimetic drugs" because they elicit from the embryo reactions which appear to be similar to those following exposure to ionizing radiations. This simply means that the embryo is a highly reactive system, responding by anomalous development to an insult, whether it be chemical or physical. The common denominator, therefore, is the embryo and not the irritant. This statement is based upon the assumption that the anomalies are in fact identical, whether caused by trypan blue or by roentgen rays. Such an assumption seems reasonable.

Since intravenously or intraperitoneally injected drugs may diffuse or be carried by the circulation throughout the body and pass through the placenta to the embryo or fetus, the dose delivered to the embryo or to its immediate environment may not be easily determined. In the case of high energy ionizing radiations, it can be assumed that ionizations probably occur rather uniformly throughout the body of the pregnant animal and its gravid uterus. Any differences in response within a litter must be attributable to intrinsic differences between the litter members, due either to hereditary (genic) or to ontogenetic (developmental) variations.

In order to study the etiology of teratologies, it was decided to concentrate upon one major anomaly, namely *exencephalia*, which is prominent and clear cut. This, anomaly is also known as cerebral hernia, pseudencephalia, "Extrakranieller Dysencephalia," "ice pack brain," or simply herniated brain in which identifiable brain tissue protrudes from the dorsum of the skull. Exencephalia is not unknown among human births (about 1/4,000) but the more extensive anomaly of anencephalia (absence of brain) seems to be more common (1/1,000).

In this study exencephalia will be produced either by roentgen irradiation of the mature spermatozoon of the mouse, or directly by exposing the developing embryo of the mouse to penetrating roentgen rays.

MATERIALS AND METHOD

This study was made from two distinct approaches. The first dealt with roentgen irradiation of the mature spermatozoon of the mouse in an attempt to produce a parthenogenetic mammalian embryo. The second was a study of the direct effects of penetrating roentgen rays on the developing mouse embryo at different stages of gestation. Since roentgen irradiation of the mature sperm or the developing embryo produced the same major teratology, namely exencephaly, these studies were combined.

In concentrating on exencephalia (cerebral hernias) there is no suggestion of bypassing as unrelated or unimportant a large variety of central nervous system and other anomalies which appear. Rather, it was felt that by concentrating on this specific anomaly, which is easily recognized and severe enough to kill the offspring, we would study the mechanism of teratogenesis in general. By dissecting the pregnant female on day 17.5 the fetuses were examined while still alive.

Preliminary studies on some 630 CF1X

* Based on work performed under Contract AT-30-1-GEN-70 for the Atomic Energy Commission.

Table I

MALFORMATIONS AMONG NORMAL OFFSPRING

CF1×CF1 mice	
Pregnancies examined at days 15.5 to 18.5	61
Total number of embryos examined	630
Total number grossly normal embryos	591 (94%)
Total number of malformed (dead) embryos)	2 (0.3%)
Total number of resorptions	37 (5.7%)
Total number of exencephalic embryos	0

CF1 implantations at 15.5 to 18.5 days were made to determine the normal incidence, if any, of this anomaly. Table 1 shows that only 5.7 per cent dead embryos were found and no exencephalies.

ROENTGEN IRRADIATION OF THE MATURE SPERMATOZOON

In 1939, it was shown that if frog sperm were irradiated with roentgen rays to 100,000 r or more and then used to fertilize eggs, the offspring were haploids and therefore the spermatozoa functioned only as parthenogenetic, stimulating agents for fertilization, making no genetic contribution to the egg or offspring. It is theoretically conceivable that the mammalian spermatozoon, similarly irradiated, might initiate development in the mammalian egg but make no genetic contribution, hence producing a parthenogenetic individual with half the requisite number of chromosomes and genetic factors. On this assumption, the following experiments were performed.

C57 black male mice, which have black coat color that is dominant over the white coat color of the CF1 mice in F_1 hybrids, were anesthetized with nembutal and shielded with $\frac{1}{4}$ inch of lead except for the scrotal testes. The testes were exposed to roentgen rays through a 16 mm. diameter aperture in lead at 19.5 cm. target distance, air dose 730 r/minute without filtration. The factors were 184 kv. peak and 30 ma. and the maximum time for exposure (60,000 r) was about 85 minutes. Exposures ranged from 10,000 r to 60,000 r and the mice were returned to their boxes to allow complete recovery.

CF1 female mice were examined by the vaginal smear method to select those which were in estrus, to supply the testes-irradiated males. As soon as the males recovered from anesthesia, they were placed each with six selected females in a single cage. On succeeding days these males were placed with other females selected for copulatory receptivity, so that each male had maximum opportunity for impregnating an appropriate female. Some of these males survived from 10 to 20 days after testes irradiation, during which matings were achieved and pregnancies followed. While all offspring appeared normal, there was a drop in litter size with exposures above 40,000 r but even at 60,000 r two litters of 8 offspring were produced. In connection with the possible parthenogenesis following testis irradiation, there was no evidence that the spermatozoa were in any way affected by the irradiation, either in motility or fertilizing power. All F_1 hybrids were dominant-black. Had the spermatozoa been so damaged by irradiation that they contributed no mutants to the zygotes, the offspring would have been white (like the mothers) if they survived at all as haploids. It is, of course, possible that some embryos were resorbed in the uteri but those which were delivered appeared perfectly normal, and all proved to be diploid (with regard to coat color) and fertile when mature.

When the F_1 hybrids were brother-sister mated to provide an F_2 generation, there was the usual black, brown, and white offspring, indicating independent assortment. Since interest at this time was directed toward embryonic anomalies (teratologies), some 73 mouse fetuses at 18 days gestation were removed and examined. None showed any gross anomaly.

The F_1 hybrids were then out-crossed to pure CF1 white stock in both directions, resulting in some 145 pregnancies of 1,292 offspring which were examined prior to the time of delivery, on day 18. This is the usual routine because the female mouse will eat any abnormal mice at birth. Of the 1,292

TABLE II

GENETIC EFFECTS: HERNIATED BRAIN PRODUCTION

Total Dose to C57 Males	$F_1 \times F_1 = F_2$ Preg./Fetuses	Exencephalies	$F_1 \times CF_1$ Preg./Fetuses	Exencephalies
10,000 r	2/0	0	32/219	2
40,150 r	7/49	0	74/714	3
50,000 r	3/16	0	33/303	0
60,000 r	2/8	0	6/56	0

offspring, representing an average litter size of 8.9, a total of only 5 (0.39 per cent) were found to have developed exencephalia or cerebral hernias (Table II). Figure 1 (Plate 1) shows the position of the litter members within the uterus and the single pronounced case of exencephaly in position R5 (right side, fifth embryo from vagina). Note also varying degrees of brain bulging from the dorsum of the skull. The pigmented eyes identify the potentially black mice, so that these brain anomalies are seen to occur in both black and white strains. In Figure 2 note the range of size and gross anomalies in the second generation from a black male who had received high level roentgen-ray exposure to the testes. This is to point up the fact that, while exencephalia is the anomaly of special interest here, numerous other anomalies will develop from roentgen-ray mutational effects. Figure 3 shows a very prominent "ice pack" type of brain protrusion. All of these were produced by roentgen irradiation altered genetic factors rather than by direct roentgen irradiation of the embryo or fetus.

ROENTGEN IRRADIATION OF THE DEVELOPING MOUSE EMBRYO

The CF1 mice were time-mated (5 P.M. to 9 A.M.) so that the pregnancies could be accurate to within several hours. Females

⟶

FIG. 1. Second generation from male C57 black mouse which had received 40,125 r to the testes, mated to normal CF1 female mouse, and hybrid F_1 mated to normal white CF1 to produce this litter. Note four embryos with dark eyes (dominant black corollary) and evidence of brain anomalies in positions L4, R1, 2, 5 with R5 being a single pronounced case of exencephaly. Anomalies in both black and white offspring, and to varying degrees within the single litter. Genetic origin following roentgen irradiation of spermatozoa, but not appearing until second generation.

FIG. 2. Another litter, similarly produced as in Figure 1, showing the range of size and other anomalies due to purely genetic factors imposed upon the grandfather.

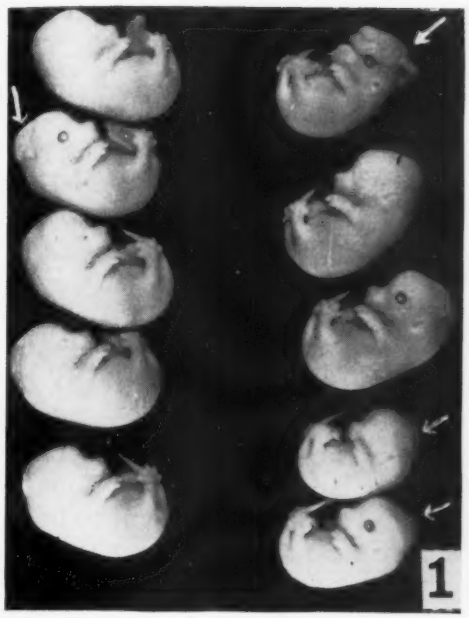
FIG. 3. Members of another litter, produced as in Figures 1 and 2, but showing only three members, two of which appear normal, but the third with a pronounced "ice pack" type of exencephalia. No evidence of excess neural development.

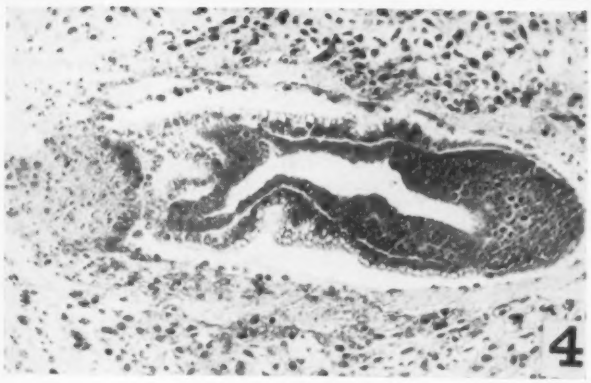
FIG. 4. Sagittal section of normal mouse embryo at 7.5 days showing large mass of embryonic ectoderm (to right) with active mitotic figures. Period of hypersensitivity of presumptive central nervous system due to abundance of neuroblasts.

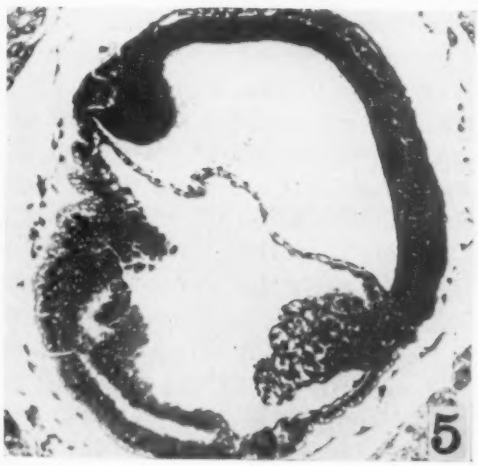
FIG. 5. Transverse section of same stage (7.5 days) showing elongated presumptive central nervous sytem as thickened mass of ectoderm with primitive streak to right, and head fold to the left. Membrane across field is amnion, above it the exocoelom and below it the amniotic cavity which in 18 day exencephalies is filled with blood. The ectoderm is the most abundant and active of the germ layers at this time.

FIG. 6. Transverse section through the embryonic neural folds at the level of the foregut, therefore presumptive mid-brain of the 8.5 day mouse embryo. Neural ectoderm is still the most definite and active of the germ layers.

FIG. 7. Enlarged view of section taken from Figure 6 showing mitotic figures and neuroblasts of the neurectoderm (presumptive central nervous system) at 8.5 days. Radiation insult or treatment with radiomimetic drugs at this time results in exencephalies and failure of the neural folds to close.







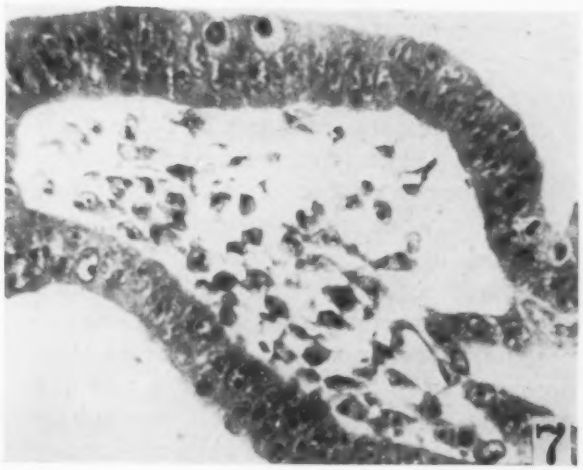


PLATE I

TABLE III

PERCENTAGE EXENCEPHALY FOLLOWING FETAL ROENTGEN IRRADIATION

Roentgen Ray Exposure	Fetal Age: Days							
	6.5	7	7.5	8	8.5	9	9.5	10
25 r	0/23	0/24	0/26	0/25	0/26	0/29	—	0/25
50 r	0/71	0/23	1/25 (4%)	2/38 (5%)	2/51 (4%)	0/19	0/11	—
100 r	0/31	0/81	0/38	0/20	0/45	1/29 (3%)	1/11 (9%)	—
150 r	0/20	0/31	2/36 (6%)	3/30 (10%)	7/32 (21%)	9/29 (31%)	0/19	—
200 r	4/82 (5%)	2/27 (7.4%)	3/86(3.5%)	7/26 (26%)	37/164 (23%)	2/26 (12%)	0/19	—
250 r	1/24 (4%)	—	—	—	—	—	0/24	0/7
300 r	1/13 (8%)	—	—	—	—	—	0/9	0/9

Formula = Exencephalies/Total number embryos (%).
Total 142 pregnancies = 1,261 offspring examined.
Average litter size = 8.1.

with vaginal plugs at 9 A.M. were removed from the mating boxes and marked for embryonic or fetal roentgen irradiation at specified times.

The irradiation facilities consisted of a single roentgen-ray tube at 36 cm. target distance from the gravid uteri, giving 100 r/min. air dose. The kv. peak was 184 and the tube was kept at 30 ma. The distance was greater than necessary, but was chosen in order to deliver a more uniform exposure to the embryos within the uteri.

Pregnant mice were irradiated, some at 6.5 days and others at various half day increments to 10 days. This covered the span of anticipated effects based upon some previous reports. A total of 142 pregnancies was studied, which had been exposed at one time between 6.5 and 10.0 days and to doses ranging from 25 to 300 r. The total number of embryos examined at 18 days was 1,261; hence the over-all litter average was 8.1. The data are shown in Table III. It can be seen that 25 r produced no cerebral hernias, but 50 r did produce 5 per cent such anomalies when the roentgen irradiation occurred on day 8. As the exposure level was increased, there was increased incidence of exencephalia so that following 200 r some cases appeared when irradiation occurred at any time from day 6.5 to day 9.0. The highest incidence of exencephaly (31 per cent) was observed when the 9.0 day mouse embryo was exposed to 150 r roentgen rays, but 8 days was a close second. In general, it appears that days 7.5 to 9.0 are the most radiosensitive with respect to this anomaly, but that this range can be extended from 6.5 to 9.0 days by increasing the exposure level. By 10 days the embryo has gone too far in development to be able to react in this particular manner so that even 300 r did not cause exencephaly.

When a gross anomaly, such as exencephalia, occurs within a litter, one always raises the question as to whether it might be the result of inadequate blood supply, anoxia due to crowding, or other transient embryologic conditions (see discussion below). For that reason further data are here presented with respect to the position within each litter of this particular anomaly, to determine whether position in the uterus or relation to other fetuses might have a causal relation apart from the roentgen irradiation. Table IV gives these data. The position of the exencephalia is designated by number from the lowest fetus, number 1, to the highest in the uterus, which might be number 8. The left and the right horns of the uterus are similarly designated, being the left and right sides of the mouse. Thus we present in this table the exact position of the appearance of the anomaly in each litter.

It will be noted that in the 24 pregnancies listed, the number of fetuses on the right was 103 and on the left 119, not significantly different. Further, some 18.4 per cent of those on the right side were exencephalic while 23.5 per cent on the left side were similarly abnormal. This, too, is not very different, so that we cannot attribute this anomaly to the uterine horn in which the embryo is implanted. A further study of

TABLE IV

POSITION AND FREQUENCY OF EXENCEPHALY IN MOUSE LITTERS AT 18 DAYS

Right Uterine Horn				Left Uterine Horn	
Total No. Embryos	Position of Exencephaly	Day	Dose	Position of Exencephaly	Total No. Embryos
7	—	6.5	200 r	3	4
5	1	6.5	250 r	—	5
0	—	6.5	300 r	2	2
6	4	7.0	200 r	—	4
6	—	7.0	200 r	2	2
5	—	7.5	50 r	2	7
8	—	7.5	150 r	3	5
5	—	7.5	150 r	3	7
2	—	7.5	200 r	7	7
2	—	8.0	50 r	8	8
7	1	8.0	50 r	—	3
2	—	8.0	50 r	8	8
7	5, 6	8.0	150 r	2	2
3	—	8.0	200 r	1, 3	6
2	—	8.0	200 r	1, 2	2
3	2	8.0	200 r	1	6
5	1, 2, 4, 5	8.5	150 r	3, 4, 6	6
4	4	8.5	200 r	2	3
7	2, 5, 6, 7	8.5	200 r	4	4
4	—	9.0	100 r	3	4
3	2, 3	9.0	150 r	6	6
3	—	9.0	150 r	6	7
3	2, 3	9.0	150 r	1, 3, 4	5
4	—	9.0	200 r	1, 6	6

Summary:
Total pregnancies = 24.
Total fetuses on left side = 119 (av. = 5).
Total fetuses on right side = 103 (av. = 4.5).
Average position exencephaly: Left side = position 3.5 (range pos. 1–8; right side = position 3.0 (range pos. 1–7).
Conclusion: Neither position in the litter nor side of uterus favored exencephaly.

the position of each anomaly within its uterine horn shows that it may occur at any position whatsoever. If one tries to determine the average position, it comes out that it is 3.5 for the left side and 3.0 for the right horn which simply means that its location may be at any level of the litter. Exencephaly, then, when occurring in litters exposed to penetrating ionizing radiations may occur in one member of a small (2) litter or five members of a litter of 11 (200 r at 8.5 days). The position in the uterus or in the litter has no bearing on the incidence of exencephaly.

Since it appears that mice at days 8.0, 8.5 and 9.0 are the most likely to react to roentgen irradiation by developing exencephalia, a study was made of the state of development of the embryonic nervous system on these days. Figure 4 is a sagittal section of a 7.5 day mouse embryo showing the most prominent mass of embryonic cells to be presumptive neural ectoderm in active mitosis. In a transverse section (Fig. 5) the long axis of the developing central nervous system can be seen, terminating to the left in the head fold around the earliest indication of the foregut. The primitive streak is to the right, continuous with the head process. Some 24 hours later, a section through the central nervous system at the level of the foregut (Fig. 6) shows normal, thickening, active neural folds with many mitotic figures (Fig. 7). It appears that the presumptive neural ectoderm, as in all vertebrates at this stage, is most active in organization and it is believed that the cells of this ectodermal layer are a mixture of neurectoderm and early neuroblasts.

Plate V encompasses the histologic and cytologic changes that follow roentgen irradiation at 7.5 days fetal age in the mouse. Figures 21–23 were taken 4 hours after roentgen irradiation and show almost immediate damage to the cellular integrity of the neural ectoderm. In all three views some loose cells may be seen within the amniotic cavity, having been discarded from the neural ectoderm. There are many dense, pyknotic nuclei and in the highest magnification (Fig. 23) hardly an intact, normal cell can be found. Figures 24–26 show the same series 24 hours after exposure, illustrating the attempt on the part of the embryo to maintain topographic integrity, clean up the cellular debris, and continue by mitosis to develop neural tissue. Some few mitotic figures are seen in Figure 25, among many badly damaged cells. In Figure 26 some rather normal cells are seen (after 24 hours), but there remain

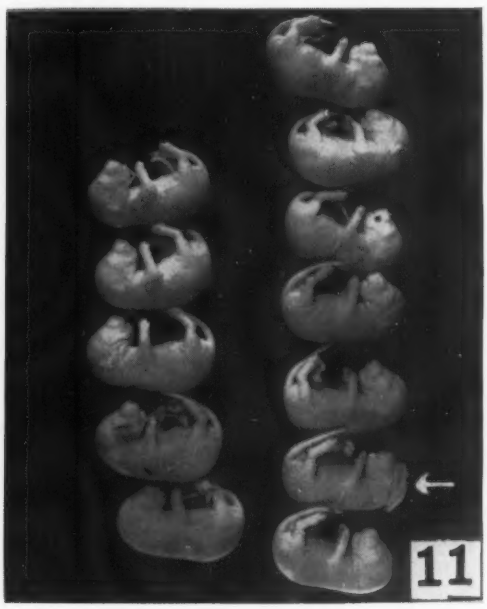


PLATE II

FIG. 8. Transverse section through the brain level of mouse embryo at 18 days, following exposure to 200 r roentgen rays at 7.5 days. Note apparently normal eyes, but much compressed cerebral vesicles and protruding brain.

FIG. 9. Mouse embryo at 18 days showing condition illustrated in Figures 8 and 10.

FIG. 10. Transverse sections through telocoele (more anteriorly than in Figure 8) but showing pyknotic and necrotic brain tissue and extensive protuberance above developing cranium. Brain vesicles almost obliterated.

FIG. 11. Lowest exposure of 50 r at 7.5 days which produced gross brain anomalies. One exencephaly at position R2. No other gross effects, not even size variations. No study was made of histologic or cytologic effects on brains of otherwise normal appearing embryos.

FIG. 12. Enlarged view of exencephaly produced by roentgen irradiation of the embryo on day 7.5. Note rather normal eye and facial contour, but gross protrusion of brain largely from the level of the mid-brain.

many pyknotic chromatin masses. Finally, if an embryo is examined 48 hours after such an irradiation insult (Fig. 27–29), it will be seen that the embryo appears rather undamaged, although (Fig. 27) the inner margins of neural ectoderm may be indistinct. The brain at the level of the otic vesicles (Fig. 28) fails to close, and this failure to close may extend to the neural tube (Fig. 29) even though the neural ectoderm appears quite normal and has many mitotic figures. Thus, we see that cellular damage is immediate, severe, and extensive, but that the embryo is able to clear away the debris (phagocytosis?) and continue its development toward a topographic whole. However, two things must be emphasized here: First, there is actual cell loss due to roentgen irradiation and, second, there is failure of the tube to close above either the brain or the cord.

A similar study was made of an 8.5 day embryo exposed to 200 r roentgen rays, and examined at 4, 24, and 48 hours thereafter. The results are presented in Plate VI. Figures 30–32 were taken at 4 hours showing extensive destruction of presumptive neural ectoderm; Figures 33–36 show the state of damage and repair at 24 hours; and Figure 37 shows a section through the brain of a 10.5 day embryo (exposed at 8.5 days) which is entirely open dorsally. The presumptive brain ectoderm is interrupted in various regions, showing incomplete repair. Such a series illustrates the influence of the "organism as a whole" to maintain its topographic integrity in the face of severe destruction and loss of its building components.

Plate II shows mouse embryos which had been irradiated at 7.5 days. The litter found in the uteri (Fig. 11) showed only one case of exencephaly resulting from a 50 r exposure, in position R2. The balance of the litter appears to be normal. Figures 9 and 12 show embryos at 18 days with this anomaly, following 200 r at 7.5 days, and Figures 8 and 10 show sections of such embryos at the level of the brain, at 18 days of fetal age. Note in these sections the disorganization of the fetal brain and its vesicles, and the protrusion of brain through what would normally develop as the skull roof. The eyes and other ventral head structures appear rather normal.

Plate III (Fig. 13 and 15) illustrates the occurrence not only of exencephalia (position L1) following 50 r on day 8, but also a much stunted embryo at position L6. When the dose at 8.5 days is increased to 200 r, such anomalies were found in 5 out of 11 members of a litter, in both uterine horns (Fig. 14). Figure 16 shows a rather normal embryo except for the one anomaly of exencephalia. The gross effects appear to be exclusively cephalic.

If the embryo is irradiated at later stages, *i.e.*, 9 days or later (Plate IV), there is still some exencephalia (Fig. 17) but it appears to be less pronounced in the individual (Fig. 18) litter member, due in all probability to some success in closing of the neural tube and overgrowth of the presumptive skull roof. Nevertheless, cerebral anomalies are in evidence, and stunted embryos can be produced (L2). Severe anomalies of the entire anterior end may ensue from a 200 r insult at 9 days (Fig. 19 and 20), involving not only the brain and exencephalia, but also including the face and lower jaws. By 9 days the embryo has developed too far to react by anencephalic changes, but the entire anterior end can be disorganized, resulting in this grotesque type of development which is limited to the cephalic structures.

Roentgen irradiation, then, can cause exencephaly either through the production of chromosomal translocations which may express themselves in this manner as early as the second generation *or* this anomaly can be produced by direct effect on the organ primordia of the central nervous system of the embryo.

DISCUSSION

In this section we will discuss the following:

A. Genetic effects relating to central nervous system anomalies

B. Ionizing radiations and the adult central nervous system
   1. Histologic effects
   2. Behavioral changes
   3. Electroencephalographic effects
C. Ionizing radiations and the human embryonic central nervous system
D. The production of animal central nervous system teratologies
   1. By chemical (drug) means
   2. By embryonic roentgen irradiation
E. Speculations as to the causative factors
   1. Significance of exencephaly
   2. Ionizing radiations and the embryo.

A. GENETIC EFFECTS RELATING TO CENTRAL NERVOUS SYSTEM ANOMALIES

The genetic cause of cerebral hernias has been known for some time,[118,119] it being suggested that the effect was due to the translocation of chromosomal material. It is difficult to ascribe to any roentgen irradiated spermatozoon a mutational change which would bring about such a specific anomaly in the second generation, but it is not difficult to believe that roentgen irradiation of the mature spermatozoon could bring about a whole gamut of mutational changes which could include this anomaly. It is within the realm of experience in experimental embryology that chromosomal effects can so interfere with the processes of gastrulation that the anterior end of the resultant embryo is distorted to the extent of either exencephaly (brain protrusion) or anencephaly (absence of brain). There is currently a study in progress showing that even 50 r to the 32 cell blastula stage can also produce exencephalic fetuses in the mouse (Rugh and Grupp—in press), probably also a result of interference with the normal processes of gastrulation. Thus, we find what the geneticists would have predicted; namely, that the immediate effect of high level roentgen irradiation of mature spermatozoa may not bring about developmental or phenotypic anomalies until after the first generation cross. It is of particular interest here that damage of the chromosomal complex of the mature spermatozoon, damage of the undifferentiated cells of the blastula (in press) and damage of the neuroblasts of the developing embryo by roentgen irradiation all affect the normal process of neurogenesis resulting in exencephalia. The common agent here is roentgen irradiation, but the common reaction is a specific type of anomalous development.

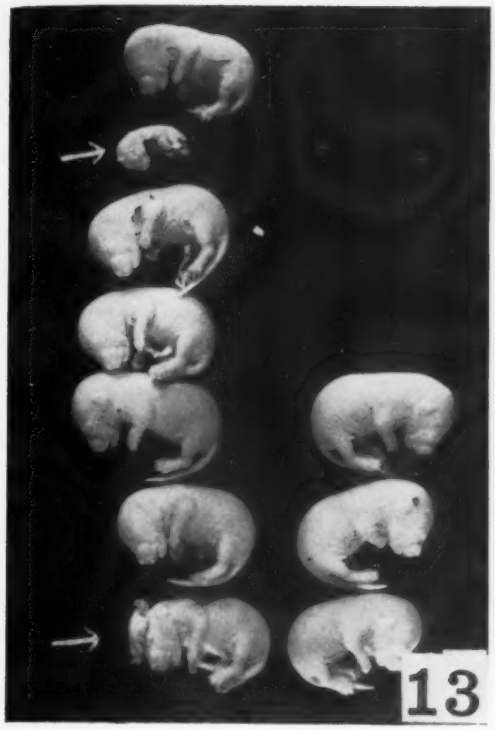
Probably the earliest study on hereditary structural defects transmitted through roentgen irradiated spermatozoa was by Bagg and Little,[3] but Snell and Dichen[118] and later Snell [119] claimed that the effects were due to chromosomal translocations which did not manifest any effect on the phenotype until the second generation. Doses of from 200–1,000 r were used and the male mice were fertile for 2 weeks thereafter. The F_1 mice were apparently normal, phenotypically, but when outcrossed produced some 38 per cent cerebral hernias in the offspring. The study reported here dealt with a much higher exposure, from 10,000 to 60,000 r, and while cerebral hernias (exencephalies) were produced in the second outcrossed generation (and not in the di-

FIG. 13. Litter of mice exposed to 50 r at 8.0 days showing one exencephaly and one stunted and deformed embryo. Exencephaly at position L1, and stunted embryo at L6.

FIG. 14. Litter of mice exposed to 200 r at 8.5 days showing higher incidence of exencephaly at positions L2, 5, 6, 7 and R4. These anomalies appear to be grossly similar.

FIG. 15. Three individuals from litter shown in Figure 13, one an apparently normal individual, one with exencephaly, and one stunted but distinguishable as an early embryo.

FIG. 16. An exencephaly from Figure 14 enlarged to show rather normal body and lower head features, but brain elements protruding through the dorsal cranium at the level of the mid-brain. These cases may be delivered alive but are invariably eaten by the mother.



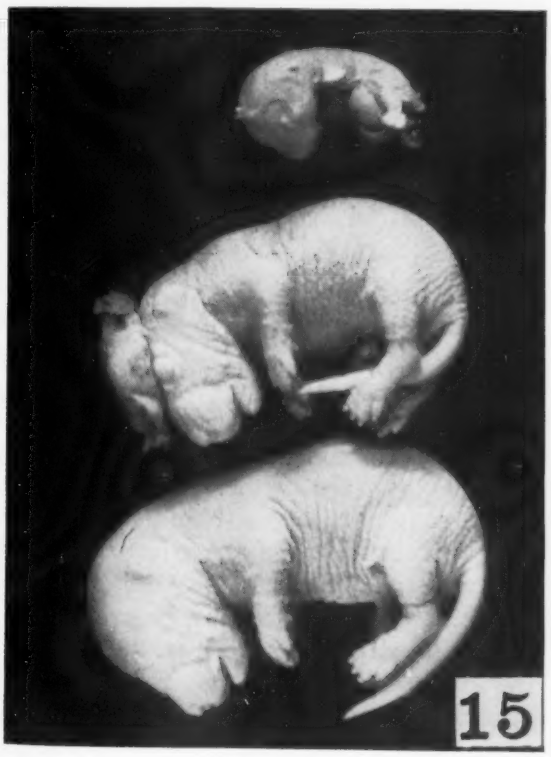


PLATE III

rect F_2), the data demonstrated that 60,000 r was not lethal for the mature spermatozoa nor did it affect either their power to fertilize normal eggs or to contribute their genes. Had parthenogenesis been achieved, by knocking out the genic complex of the mature sperm of the C57 black males, the offspring of the CF1 white females would have been white. They were invariably black, normal-sized litters, and fertile.

Neel *et al.*[92] studied children who had been exposed in utero at Hiroshima and Nagasaki and found that the genetic effects were exactly what would have been expected from plant and animal studies. In another report Neel *et al.*[92] state that the "Public hazard in the first generation offspring of exposed parents appears to be slight" and "There is no indication from this study that the sensitivity of the human genes to radiation is not comparable to that of experimental plants and animals used in radiation experiments." There was an increase in the stillbirths, a decrease in the livebirth weights, some possible effect on the sex ratios, some increase in malformations, and an increase in the neonatal and infant deaths. Based upon the mouse studies reported here, it will be important to delay any final analysis of human effects at least until succeeding generations appear. Otis[95] found that irradiation induced translocations caused prenatal loss, greatest at the time of implantation in the mouse, but that corkscrew spinal cords, open metencephalon and myelencephalon, and everted central nervous tissue were all produced as a result of exposure of the germ cell (not the embryo). Finally, Muller[80] again pointed out that there is no threshold dose to the gonads, and that all doses must be considered as carrying some risk. It has been found that it is the total accumulated dose, not its intensity nor its duration, that is effective and that the frequency of mutations induced by roentgen irradiation (of the germ cells) is proportional to the dose received. Thus, the mature spermatozoa which were used to produce the hybrid F_1 generation in the experiments reported here must have carried almost the maximum of possible mutations, chromosomal breaks, and translocations, simply because of the magnitude of the exposure. Nevertheless, the F_1 appeared to be normal because the unirradiated CF1 female contributed to each of the F_1 offspring what was functionally a normal, or more normal, allelomorph for each possible deleterious roentgen irradiation induced mutation contributed by the spermatozoa. However, when the F_1 hybrids were outcrossed to CF1 normals, the 40,000 r to the grandfather began to express itself in a variety of anomalies in the offspring, including 3 cases of cerebral hernias out of 714 mice. Other anomalies far outnumbered this single object of study, exencephaly. Since these herniated brains were of genetic origin, the only mechanism by which they could be produced would be by interference with the process of gastrulation and the consequent cephalic disruptions. Such interference would be expected from extensive chromosomal imbalance.

B. IONIZING RADIATIONS AND THE ADULT CENTRAL NERVOUS SYSTEM

(1) The adult brain has been presumed to be relatively very radioresistant, but the studies of local roentgen irradiation have not been at all conclusive. There have been numerous histologic and cytologic studies following direct irradiation of the adult mammalian brain, either whole or in part. Two patients, receiving 6,000 r and 3,500 r respectively, to limited regions of the brain, subsequently developed brain lesions and "amyloid" type of degeneration.[77] Another patient was given 2,500 r to the right temporal scalp with the subsequent development of a brain lesion necessitating a right temporal craniotomy.[23] Those reporting the case believe that irradiation caused progressive, obliterative vascular disease suggesting amyloid degeneration. Arnold *et al.*,[1] in studying betatron exposure of the monkey brain, stated that the central nervous system of both monkey and man is more radioresponsive than is generally supposed.

Plate IV

Fig. 17. Mouse embryos exposed to 150 r at 9 days showing (at 18 days) two normals, five exencephalies, and one abortive embryo. Total gross anomalies equal 72 per cent. No histologic study was made of the two apparently normal fetuses.

Fig. 18. Similar to Figure 17 (irradiated at 9 days) but exposed to 200 r. In this case there were two exencephalies and one stunted embryo, position L2, with total of 30 per cent anomalies.

Fig. 19 and 20. Single mouse embryo at 18 days which had been exposed to 200 r at 9 days' gestation showing severe cepahlic anomalies not only including exencephaly but distortions of the face and lower jaw. In this instance the eyes are not seen, but note the normal appearance of the balance of the body posterior to the head.

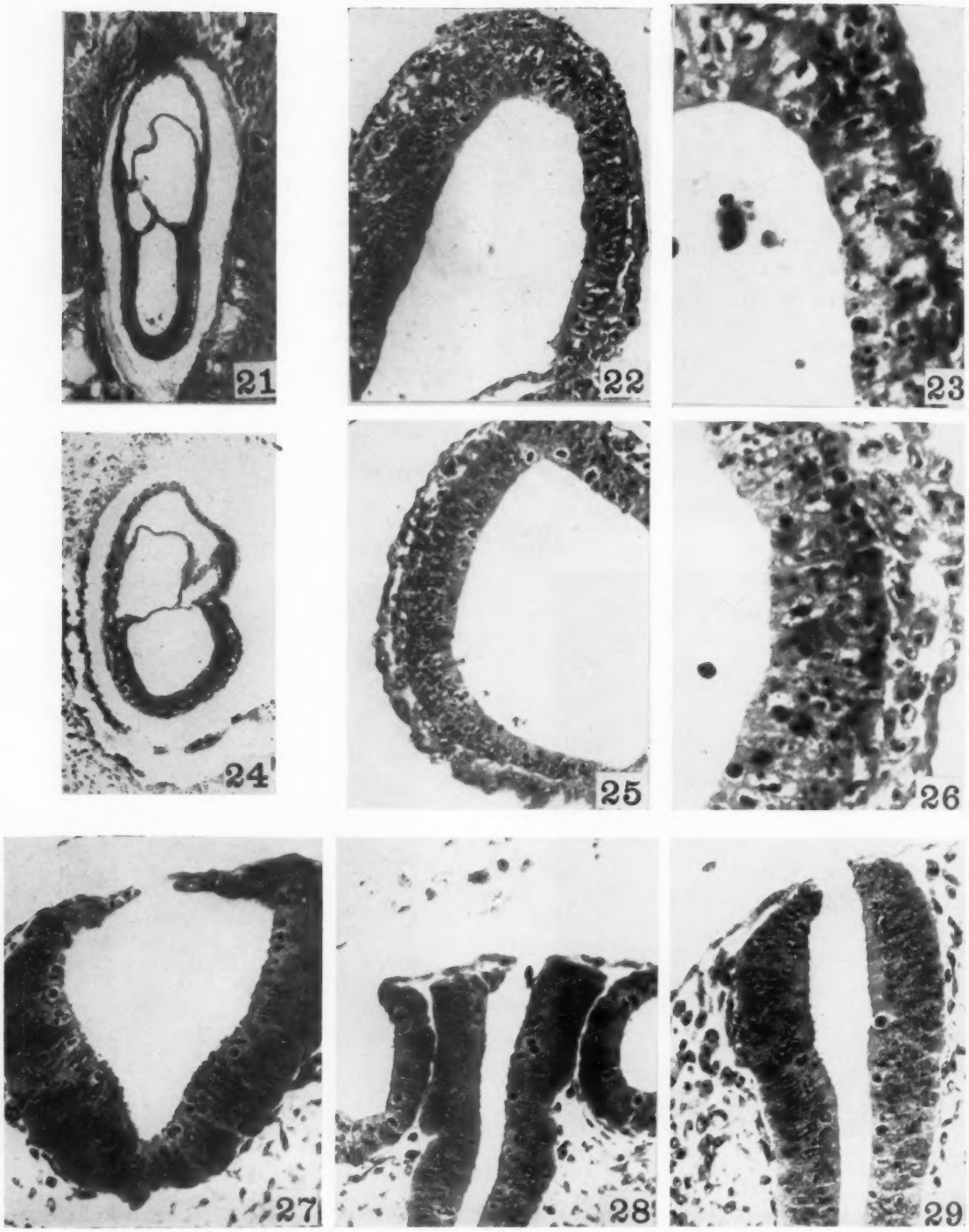


PLATE V

FIG. 21. Section of mouse embryo in uterus at 7.5 days, 4 hours after being exposed to 200 r. Gross topography is normal, with ectoplacental cone above and thick neurectoderm below, surrounding the proamniotic cavity.

FIG. 22. Enlarged view of embryo shown in Figure 21 but limited to the anterior end showing severe pyknosis and cell destruction at 4 hours after exposure to 200 r at 7.5 days.

(*Continued on facing page*)

There is a radioselectivity on the part of the white matter of the adult, and the glial cells are adversely affected by irradiation. These workers believe the effects are direct on the nervous elements and not mediated through vascular degeneration. But, since irradiation can produce delayed necrosis, irradiation of the central nervous system must be thoroughly controlled, particularly with regard to the possibility of exposure of the brain stem. Clemente and Holst[15] produced extensive neuronal pathology and neurologic disorders by irradiating the heads of monkeys and stated that the primary impairment was of neurons, neuroglia, and the vascular system. The hypothalamus and medulla were particularly vulnerable when doses of 4,500 or more were used. Another case in which 6,600 r was given in 20 days included the spinal cord and resulted in death in three months. Autopsy showed demyelinization of the white matter of the cervical spinal cord and some gliosis in the gray matter (Boldrey, Welch and Fadell, 1954). Gerstner *et al.*[29] exposed the brain of rabbits to 14,000 r and caused changes as early as 3 hours, including changes in water content, specific gravity, vasculitis, and pyknosis of granular cells of cerebellum. Later, Gerstner and Kent[30] found 100 per cent pyknosis of the cerebellar granular cells after 9,000 r to the head of rabbits. Lower doses caused progressive apathy and other degenerative effects. But Hicks[54] revived the conviction that radiation damage to the adult central nervous system is a secondary late effect that results from slowly developing vascular damage. After high dosage, acute endothelial damage with thrombosis may account for parenchymal changes. Only the radiations reaching the brain are effective; those to the body bear no relation to central nervous system damage.[124] Brain exposure of the monkey shows histologic effects within 2 hours, reaching a peak in 8–24 hours, and regressing. Pyknosis of cerebellar granular cells was pronounced. Brownson and Moss[12] gave 1,600 r to the brain of the guinea pig to find a reduction in the perineuronal glial satellite cells, a decrease in microglia and increase in oligodendroglia. Neurons showed conspicuous Feulgen positive granules. Thus, while it was originally thought that the adult mammalian brain was relatively very radioresistant, it is now believed that it is not so immune but the exact place of the blood-brain barrier in this sensitivity has not been determined.

(2) Behavioral studies by Kaplan[61] showed that even a lethal exposure (1,000 r) of the monkey did not destroy its memory for a learned task until shortly before its death (151 hours). When rats, guinea pigs,

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Fig. 23. Further enlargement of section of neurectoderm and neuroblasts showing abundant pyknosis, sloughing off of dead cells into the proamnion, extensive vacuolization, and very few intact cells.

Fig. 24. Section of mouse embryo 24 hours after exposure to 200 r at 7.5 days' gestation. General topography quite normal but development not as far as one would expect for 8.5 days. Embryonic ectoderm appears to be disorganized.

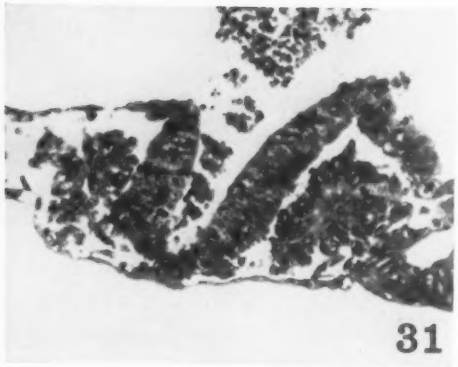
Fig. 25. Enlarged view of section of neurectoderm from Figure 24. Note few mitotic figures appearing 24 hours after exposure, among many pyknotic nuclei and disorganized cells. Compare with Figure 7.

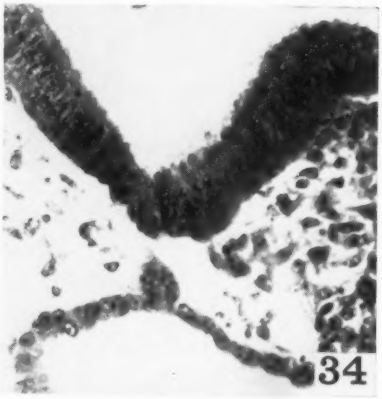
Fig. 26. Further enlargement to show cellular detail from Figure 24. Note discarded nucleus in proamniotic cavity and other hyperchromatic nuclei, but appearance of a few apparently normal cells which survived the radiation insult. These are probably neurectoderm, immune to roentgen irradiation, and the precursors of any apparently normal ectodermal derivatives.

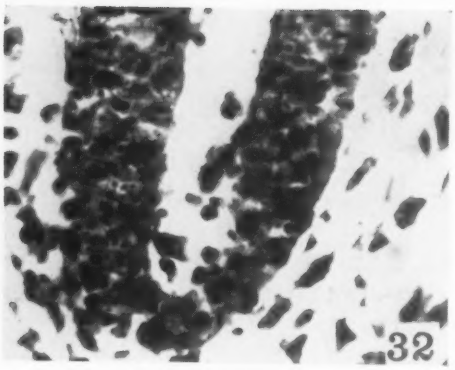
Fig. 27. Section of mouse embryo after exposure to 200 r at 7.5 days' gestation showing resumption of development and rather intact neural ectoderm with many mitotic figures. This section is at the level of the mesencephalon and the folds were interrupted dorsally in every section. Note also the frilled aspect of the lining neurectoderm and residual damaged nuclei more peripherally located.

Fig. 28. Similar to Figure 27 but section taken at the level of the otic vesicles. Here also the neural folds above failed to close over, but the neurectoderm appears largely intact with mitotic figures.

Fig. 29. Similar to Figures 27 and 28 but at the level of the spinal cord showing failure of the folds to close above, some frilled cells lining the neurocoele, but few mitotic figures.







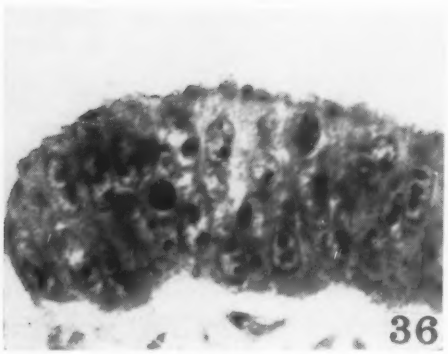


PLATE VI

FIG. 30. Neural groove at the level of the pericardial coelom of the mouse embryo at 4 hours after being exposed to 200 r at 8.5 days' gestation, showing abundant loose neural cells in presumptive neural groove

(*Continued on facing page*)

and hamsters were exposed to the $LD_{50/30}$ level of roentgen rays[13] the survivors showed depressed activity, with a second depression at 3–4 weeks. However, these workers attributed the species differences to differences in sensitivity of their gastrointestinal tracts rather than to effects directly on their nervous systems. Roentgen irradiation of dogs (total body) to 300 r caused "behavioral decay,"[18] with decreased efficiency of adaptive behavior not related to reduction in appetite.

Kimeldorf *et al.*[67] have shown that 30 r to the rat, 354 r to the mouse, or 318 r to the cat (delivered over 3 days) will condition them to avoidance behavior. Finally, while 400 r reduced the volitional activity of adult rats within 2–3 weeks, if 650 r was given, followed by bone marrow injection, the behavior of the rats was similar to that of the controls with no reduction in volitional activity.[60] Thus, it appears that some chemical agents may "protect" the central nervous system at certain levels of exposure at least.

Studies of the behavior of fetally-irradiated rodents during their subsequent adult life showed that the learning ability of rats was decreased as a function of the radiation exposure, variability in performance was increased, and that rats irradiated on gestation day 13 were the most adversely affected.[74] Such rats were very nervous in any maze situation with chattering teeth, persistent scratching, face washing, defecation, urination, and were difficult to tame. These findings were confirmed for the mouse, where it was shown that 100 r given on days 12.5 or 13.5 to the embryo produced individuals that were hyperexcitable when stimulated electrically.[109]

(3) Electroencephalographic studies are difficult to analyze when made on lower mammals, but may, nevertheless, be very significant. In higher mammals (monkeys) whole body exposure in the lethal range shows an electroencephalographic pattern in the preterminal stage with "high voltage, slow waves, which gives way to an almost isoelectric tracing before death."[19] This led the investigators to state that the central nervous system has a very high degree of resistance to roentgen irradiation. Similar observations were made by Ross *et al.*[103] The cerebellar response in cats[73] tested during irradiation showed decrease at about 6,000 r and a severe flattening after 10,000 r. Further electroencephalographic studies on the monkey[11] showed effects within several minutes of the initiation of exposure. There was generally a recovery which persisted. The general effect on the electroencephalogram was a decrease in wave frequency and voltage. The initial transient suppression of electrical activity (effect on neural function) is followed by a subsequent

being sloughed off after radiation insult. Endoderm and mesoderm appear normal.

FIG. 31. Enlarged view of Figure 30 but more posteriorly, showing extensive pyknosis in neural groove ectoderm and possibly slight effect on lateral somite mesoderm. A few mitotic figures may be seen at this time.

FIG. 32. Further enlargement of the neural groove section showing almost complete disorganization of the embryonic ectoderm.

FIG. 33. Section of mouse embryo 24 hours after being exposed to 200 r showing level of heart, wide open neural groove above, and dense neurectoderm.

FIG. 34. Similar to Figure 33 but enlarged to show destruction of cell margins toward the presumptive neurocoele but no sloughed off cells in the vicinity, very few pyknotic nuclei, and intact notochord, endoderm and mesoderm.

FIG. 35. Similar to Figures 33 and 34 but at the level of the neural tube showing failure of the neural folds to close above, but some apparently normal cells within the neural ectoderm.

FIG. 36. Oil immersion view of neural ectoderm from Figures 33, 34 and 35 showing few remaining abnormal nuclei among many neurectoderm cells which are becoming neuroblasts in the differentiation process.

FIG. 37. Level of telencephalon of mouse embryo 48 hours after being exposed to 200 r at 8.5 days' gestation, showing rather intact neural ectoderm of the brain (except in limited areas) but persistent dorsal opening above where the choroid plexus should be found. The third ventricle is to the left, with lateral ventricles on either side. Exencephaly may be due to failure of dorsal ectoderm to close over, or to failure of the mesenchymal cranium to develop, or to both factors.

more extreme loss of activity which may be related to other bodily functions.

Therefore, numerous studies have indicated that on the basis of histologic, behavioral and electroencephalographic changes subsequent to roentgen irradiation of the adult brain, there is more damage even at lower levels of exposure than originally believed. Whether still lower exposures (*e.g.*, diagnostic levels) might have perceptible effects by any tests cannot be stated at this time. However, it is still apparent that the adult brain (or neuron) is much more resistant to ionizing radiations than is the fetal brain (or neuroblast) by any test applied.

C. IONIZING RADIATIONS AND THE HUMAN EMBRYONIC CENTRAL NERVOUS SYSTEM

Let us then examine what is known about roentgen irradiation effects on the central nervous system of the human embryo. Naturally data are scarce, and limited to those who are alert to the situation and are willing to report their findings in the scientific literature.

Human teratologies of the central nervous system, caused by exposure to ionizing radiations, have often appeared in the literature, beginning probably with the report of Murphy[89] who linked maternal pelvic irradiation with subsequent microcephaly. Goldstein and Murphy[42,89,90] reported that radium treatment of cervical cancer during pregnancy caused micromelia and microcephalic idiocy. Numerous congenital malformations, including 366 anencephalies, were analyzed by Record and McKeown[100] but no attempt was made to correlate these with histories of roentgen irradiation.

A few individual cases will emphasize the problem of getting reliable exposure data relative to the teratologies. Hobbs[57] reported a male exposed in utero to 900 r who appeared to be quite normal at 18 months. However, at a later date there appeared to be evidence of neurologic involvements. Koch[68] reported a child irradiated with roentgen rays during gestation who showed marked mental and physical underdevelopment, but there were others who appeared normal. An exposure of 200 r at two weeks' pregnancy seemed to have no effect on a child,[102] but roentgen-ray examinations of a pregnant woman at 4, 5 and 6 months for diagnostic purposes resulted in a child with microphthalmus, microcornea, syndactyly, strabismus, hypermetropia, amelogenesis, and odontogenesis imperfecta.[98] Roentgen therapy for castration at the fourth month of an unrecognized pregnancy was thought to be the cause of the child being microcephalic, hydrocephalic, and porencephalic. Psychometric tests showed complete idiocy.[5] It would help in the final evaluation of this entire problem if clinicians would document the cases that come to their attention, checking particularly the dosimetry, total fetal exposure, and exact embryonic or fetal age.

The hazards to the human embryo, based largely upon rodent studies and cautious extrapolations, were suggested by Russell and Russell.[113,116] It was shown that an exposure of as little as 35 r might be critical for the human embryo at certain stages, particularly during the first trimester. Patten[96] reviewed human cases of neural tube overgrowth which might lead to anencephaly or exencephaly.

The atomic bomb studies at Hiroshima and Nagasaki have led to certain definite correlations of the effect of ionizing radiations and fetal (congenital) anomalies. Of 11 children within 1,200 meters of ground zero (Hiroshima) during intrauterine development, 7 showed microcephaly with mental retardation.[99] Sutow, Hamada, and Kawamoto[123] found that children close to ground zero (Nagasaki) showed more neurologic anomalies than did the more distant controls, but they did not find the types of anomalies generally attributed to fetal roentgen irradiation of rodents. Kawamoto *et al.*[63] found the head circumference of males exposed in utero to be considerably more reduced by irradiation than the heads of the sibling females. Later Kawamoto[64] stated that while the physical fitness of children exposed at Nagasaki was not ap-

preciably different from that of the controls, it would be well to await studies when the children were somewhat older. Yamazaki, Wright and Wright[143] found 30 mothers who had been severely exposed to the bomb irradiations at Nagasaki, and among their children, exposed in utero, there were 23.4 per cent fetal deaths, 26 per cent neonatal and infant deaths, and 25 per cent mental retardation among the surviving children. A study at 9 years confirmed the statements that the nearer the embryos or fetuses were to ground zero at the time of detonation, the greater the likelihood of microcephalia appearing with its attendant mental retardation.[79] A very exhaustive study was made by Neel and Schull[93] on 76,626 postwar pregnancies which showed impairment of growth in anthropomorphic measurements, but the authors imply that such a study must await later analyses before any conclusions can be drawn. This may require several generations. Finally, Stewart *et al.*[120] made a survey of malignant disease in children, reporting 11.9 per cent of children irradiated in utero developing anomalies of the central nervous system. There is no doubt but that the nervous system of the embryo, be it rodent or anthropoid, is sensitive to ionizing radiations in such a manner as to develop anomalies from mild necrosis to anencephaly. There is no information on functional effects below those which have anatomic corollaries.

Anencephaly of the human was probably first described by Lebedeff[72] in 1881 as due to disorders in connection with the primary flexures of the brain. Later[122] it was thought to arise from nonclosure of the neural tube which is continuous with the brain, or possibly from the actual rupture of the brain stem following excessive pressure of the cerebrospinal fluid.[24] Erskine[20] offered the developmental explanation that the mesoderm underlying the embryonic ectoderm, which normally tends to organize the ectoderm into neural primordia, is affected in some way and that secondarily the developing brain becomes abnormal. This type of explanation would fit the genetic causes better, since they precede the development of any neural primordia.

D. The production of animal central nervous system teratologies

(1) The mammalian embryo appears to be readily affected by certain drugs (chemical compounds) injected either intraperitoneally or intravenously into the pregnant animal, or by hypoxia and anoxia. A wide variety of anomalies have been produced in mice and rat embryos, particularly by trypan blue, and many of these anomalies involve the central nervous system, including exencephaly and anencephaly. For those particularly interested, the references are given in Table v. The italicized references are those in which exencephaly or a closely related condition has been produced.

While exencephaly and anencephaly are found among otherwise normal human births, there has been no evidence as to their cause, whether by ionizing radiations, chemical agents, or other possible factors. The above chemicals are sometimes designated as "radiomimetic" simply because they elicit from the developing embryo the same types of reaction that follow exposure to ionizing radiations.

(2) Probably the first description of radiation induced anomalies in experimental animals was given by Baily and Bagg.[4] Kaven,[65,66] who roentgenographed pregnant mice between 7 and 19 days, found the cephalic anomalies to be the most frequent including exencephalies. He produced brain hernias ("Extrakranieller Dysencephalia") in 10 per cent of the fetuses by exposing the embryos between days 13–16, and only 2.4 per cent when the fetal mice were irradiated between 17–19 days, at doses as low as 178 r. Kaven stated that exposure on day 8 affected the encephalon; day 12 caused hydrocephaly; day 14 resulted in sterilization; and day 18 caused cataract development. Both Kaven[65,66] and later Russell[110] have suggested that exposures before day 8 did not cause anomalies in the surviving mice. When 300 r was given on day 10.5, it produced the same result,

TABLE V

PRODUCTION OF BRAIN ANOMALIES IN THE FETUS, FROM NECROSIS TO ANENCEPHALY, BY TREATMENT OF THE PREGNANT RODENT (MOUSE OR RAT) BY CHEMICALS

TRYPAN BLUE: Gilbert and Gillman,[31] 1948; *Murakami and Kameyama*,[81] 1950; *Murakami*,[82,87] 1952, 1957; Waddington and Carter,[126] 1952; Hamburgh,[44,45] 1952, 1954; Harm,[46] 1954; *Murakami, Kameyama, and Kato*,[84,86] 1954, 1956; Wilson (rabbits),[141] 1955; Ferm,[22] 1956; Gunberg (rats),[43] 1956; Fox and Goss,[25] 1956; Waddington and Perry (amphibia),[125] 1956; Beaudoin and Wilson (chicks),[7] 1958; Wilson,[142] 1957.

AZO BLUE: *Wilson*,[139] 1954.

LITHIUM CARMINE: *Murakami*,[82,87] 1952, 1957; *Murakami, Kameyama, and Kato*,[84,86] 1954, 1956; *Murakami and Katsunuma*,[85] 1955.

VITAMIN A: (deficiency) Warkany, Nelson, and Schraffenberger,[127] 1943; Warkany and Schraffenberger,[130] 1947; Warkany,[129] 1947; Warkany and Roth,[131] 1948; Wilson and Warkany,[133,134,135] 1948, 1949, 1950; (excesses of vitamin A) *Cohlan*,[16] 1953; *Giroud and Martinet*,[38,39] 1956, 1957.

PANTOTHENIC ACID DEFICIENCY: Boisselot,[8,9,10] 1948, 1949, 1951; *Giroud*,[36,37] 1953, 1954; *Giroud, Delmas, Prost, and Lefebvres*,[40] 1957.

CORTISONE: Baxter and Fraser,[6] 1950; Fraser and Fainstat,[27] 1951; Fraser, Fainstat, and Kalter,[28] 1953; Strean and Peer,[121] 1956.

FOLIC ACID DEFICIENCY: Giroud and Lefebvres-Boisselot,[34] 1951; Evans, Nelson, and Asling,[21] 1951.

RIBOFLAVIN: Warkany,[128] 1944; Warkany and Schraffenberger,[130] 1947; Giroud and Boisselot,[32,33] 1947, 1948.

INSULIN: Lichtenstein, Huest, and Warkany,[75] 1951; Hicks (hypoglycemia),[52] 1953.

NITROGEN MUSTARD: Haskin,[47] 1948.

FUEL GAS: Murakami, Kameyama, and Kato,[86] 1956.

ANOXIA: *Ingalls, Curley, and Prindle*,[58] 1950; Hicks,[52] 1953.

HYPOXIA: Rubsaamen (chick),[104] 1950; *Murakami and Kameyama*,[83] 1954. (No deleterious effects) Russell, Russell, and Major,[112] 1951; Russell and Russell,[114] 1954.

VARIOUS DRUGS: (TEM, Aminopterin, Malanonitrile, Plasmacid, Flouactetate, Mepharsen, Iosobenzoate, and Chlormercuribenzoate) Hicks,[49,52] 1952, 1953.

due to a defective (skeleton) cranium.[113] In a series of studies on the rat embryo, Hicks[48–55] found no deleterious effects below 100 r, but evidence of neuronecrosis following 150 r during the "second and third week of gestation." Rat embryos exposed to 150 r at 9 days showed anencephaly, or total absence of brain, but in no case was exencephalia described. Possibly this does not occur in the rat. Hicks emphasizes that "complete or near complete repair can occur in many zones."

In 1957 Murakami[87] and co-workers produced the same type of cerebral hernia by treating pregnant mice with trypan blue, lithium carmine, or roentgen rays. They found day 13 to be the most susceptible.

Table VI gives the references to those papers in which cephalic anomalies have been described, following embryonic or fetal roentgen irradiation. The italicized references are those in which exencephaly has been described.

Roentgen rays are nonselective, penetrating all tissues and organs, while chemical substances may concentrate in one region or another.

In all instances when an irradiated, pregnant mouse was opened at 17–18 days for examination of its fetuses, it was possible to immediately locate those litter members which would show exencephaly. Each one was invariably enclosed in an amniotic sac filled with blood. Such fetuses were alive, having developed otherwise normally, but would have been destroyed by the mother at birth. They could not have survived, in any case.

In order to understand the embryologic aspects of this problem, it would be well to describe briefly the major dynamic changes

TABLE VI

THE PRODUCTION OF CEREBRAL ANOMALIES BY EXPOSING THE EMBRYO TO IONIZING RADIATIONS

De Nobele and Lams[17] 1925; Kosaka,[69–71] 1927, 1928, 1929; Murphy and de Renyi,[91] 1930; Job, Leibold, and Fitzmaurice,[59] 1935; *Kaven*,[65] 1938 (2); *Warkany and Schraffenberger*,[130] 1947; *Rugh (amphibia)*[105,109] 1949, 1956; Hicks,[48–53] 1950, 1952, 1953; *Russell*,[110,111] 1950, 1957; Wilson,[136,140] 1952, 1954; *Wilson and Karr*,[137] 1951; *Wilson, Jordan, and Brent*,[138] 1953; *Murakami and Katsunuma*,[85] 1955; Chapman and Latta (chick-P^{32}),[14] 1956; *Riggs, McGrath, and Schwartz*,[101] 1956; *Murakami*,[87] 1957; *Murakami and Kameyama*,[88] 1958.

that occur in the rodent (mouse) embryo over this critical period.

At 6.5 days: All of the primary germ layers are laid down, implantation has begun, and the embryo is bathed in maternal blood.

At 7.0 days: Implantation is essentially completed. The embryo consists of a head process, primitive streak, allantois, yolk sac, amniotic folds, and exocoelom.

At 7.5 days: The primitive streak and head process are the most prominent and actively developing structures, but the neural groove and notochord are forming, head mesenchyme appears, blood islets develop, the foregut is a mere pouch, and there are three prominent cavities (amnion, exocoelom, and ectoplacenta). The decidual growth tends to isolate the embryo into its crypt.

At 8.0 days: There is obvious cephalization, or accentuated growth of the anterior structures. The first (anterior) somites appear lateral to the developing neural tube, the stomodeum and hindgut are distinguishable, the yolk sac envelopes the amnion and exocoelom, and the uterine cavity is quite completely blocked off by the implantation mass.

At 8.5 days: The cephalic flexures develop, eleven somites have appeared, the neural tube is closing along its entire length, the brain vesicles are distinguishable, branchial arches and heart appear.

It is obvious from this chronology that the time of maximum probability of producing exencephalic embryos in the rodent correlates well with the very active development of the cephalic structures, the head mesenchyme, the brain and neural tube. The embryonic ectoderm at this time is changing from a rather flat plate of undifferentiated cells to a groove and then to a tube which immediately transforms into a multivesicle brain and long neural tube. The cells of the neurectoderm which will actively participate in this brain and spinal cord formation are the ones which manifest the maximum damage in the histologic study reported here. Since many, if not all, of the damaged cells are sloughed off and discarded, what remains is insufficient in mass to form a complete brain and cord, and also may be inadequate in the developmental potencies necessary to accomplish normal neurogenesis. The reason for cephalic damage without equivalent effects on the rest of the developing embryo is that, at the time of roentgen irradiation insult, the morphogenetic forces of the anterior end (organizers) are the most active and involve many metamorphic (neuroblast) cells.

It has been stated that congenital defects are the third ranking cause of infant deaths.[76] These teratologies (congenital anomalies associated with development) could arise from a variety of influences which may involve according to Patten:[97] (a) Developmental arrest; (b) retarded growth; (c) altered resorption (too much or too little); (d) abnormal location for resorption; (e) abnormal location for growth; and (f) local overgrowth but not neoplastic. In this latter category is myeloschisis in which case the neural plate tissue is so voluminous that the normal overgrowth of covering tissue cannot develop. It is very possible that some cases of exencephaly can be thus classified, although there is little evidence of actual increase of neural volume in these roentgen irradiation studies. Damage to the neuroblasts, resulting in depletion of cells, is such that there is failure of the neural groove to close above, particularly at the level of the brain. This closure and overgrowth of skeleton is normally aided by mesenchyme. Consequently, when the brain ectoderm grows, it is not restricted and tends to extend beyond the limits of the cranium. Thus, we have protrusions of the brain which persist. Some litter members appear to be able to tolerate the same exposure without such protrusions, but it is not to be presumed that such individuals are devoid of neurologic damage of comparable nature which might have widespread functional sequelae.

Brief mention is made here of two references to the effect that the placenta might

be a contributing factor in maldevelopment of irradiated or drug-exposed fetuses,[62,82] but this has been denied both by Russell,[110] Russell and Russell,[114] and by Hicks.[50–53] Effects of ionizing radiations are directed to the fetus, not mediated through the placenta or the mother, both of which are more radioresistant than is the embryo.

E. SPECULATIONS AS TO THE CAUSATIVE FACTORS

(1) Exencephaly is but one of many possible results of developmental disruption, incurred at a time when the brain (and cephalic structures in general) is being laid down in the embryo. It is believed that the neuroblasts, precursors of the neurons, are extremely radiosensitive and these cells are in abundance beginning about the seventh day of gestation in the mouse. This compares with about 16–18 days in the human. Thereafter, neuroblasts are present in embryos until and after the time of birth, and wherever they are, they are vulnerable, probably to some of these radiomimetic chemicals as well as to ionizing radiations since exencephalies can be produced by either agent. As soon as these neuroblasts differentiate into neurons, they become relatively more radioresistant, so that teratologies of the nature of exencephaly cannot be produced. The nature of the ultimate damage will depend more on the time of insult than on the degree of exposure, within limits. It should not be presumed that the neuroblasts alone are so sensitive, for the mesenchyme (primitive mesoderm) of the embryo is also in a formative stage and is probably similarly radiosensitive. These mesenchyme cells, precursors of the skeletal mesoderm, are involved not only in neurogenesis but in developing the enclosing skull and vertebral column.

(2) For some time it was thought that the embryo was able to repair and recover such damage as was incurred by ionizing radiations or by radiomimetic drugs. This was due in part to the fact that there was usually a delay in the study of effects until birth or thereafter, and surviving animals did indeed appear to be topographically normal. However, it has been shown that in the case of the neural retina,[106,107] while the eye of the fetally-irradiated mouse may appear topographically normal after birth, it was reduced in size in rough proportion to the degree of irradiation during embryonic life. Thus, from the exencephalies reported here to the microcephalies reported from Hiroshima and Nagasaki, we are dealing with neural deletions due to exposure to ionizing radiations during embryonic life. These are gross anomalies, easily detected and measured. We do not yet know the level of insult to the embryo which will show electroencephalographic, behavioral, or even psychologic sequelae not correlated with gross or histologic manifestations. Certainly, this undetermined area is of vital importance not only to the medical profession, particularly radiologists who might be called upon to irradiate embryos, but to those concerned with the mental fitness of the general population.

One cannot safely extrapolate scientific observations from a rodent embryo to the embryo of the human, nor can one draw any direct conclusions from one to the other. Nevertheless, as Otis and Brent[94] have shown, it is possible to compile a graph of equivalent stages of development of the mouse and the human embryo and find a very smooth curve, indicating that the chronology of development is essentially the same. With the support of fundamental embryology and scattered references to anomalies in the human, similar to those induced by roentgen irradiation of the mouse or rat embryo, it is legitimate to suggest that, at least until more facts are known, it would be very wise to reduce the instances of human embryonic and fetal exposure to penetrating ionizing radiation to an absolute minimum.

SUMMARY AND CONCLUSIONS

1. The incidence of resorptions among 630 untreated offspring of normal CF1 mice, examined at 17.5 days gestation, was

5.7 per cent, and no exencephalies (cerebral hernias) appeared.

2. The mature spermatozoa of C57 black mice can tolerate 60,000 r roentgen rays and still be motile and fertile, producing normal offspring in hybrid crosses with CF1 females. These hybrids are fertile but must carry chromosomal translocations because in the subsequent generation exencephalies (cerebral hernias) appeared among a variety of anomalies.

3. When CF1×CF1 pregnant mice were roentgen irradiated on days 7.5 or 8.0 with 50 r, exencephalies were produced. When the exposure was increased to 200 r, the incidence of this central nervous system anomaly was increased to 26 per cent following exposure on day 8.0. Also, at this higher level of exposure the anomaly occurred following roentgen irradiation at any time from day 6.5 to 9.0. By 10 days' gestation even 300 r did not produce this anomaly, since the embryo had developed beyond the stage of closure of the neural tube and brain vesicles.

4. There is no evidence that either uterine horn or position in the uterus of any litter member was in any way related to the production of this anomaly. In every litter in which exencephaly developed, there were normal appearing litter mates. It is presumed that these mice, though not showing the gross teratology of exencephaly, nevertheless would exhibit by other tests effects of serious neurologic injury.

5. The mouse embryo at 7.5–8.5 days is made up largely of neurectoderm which is actively transforming, through neuroblasts, into neurons of the central nervous system tissue. It is these neuroblasts that are so radiosensitive. Four hours after exposure many of them are seen to be necrotic or even pyknotic. By 24 hours mitosis is resumed and by 48 hours the embryonic central nervous system appears to be topographically normal. It is, however, deficient to the degree of necrosis and pyknosis.

6. Exencephaly in the mouse following embryonic roentgen irradiation apparently develops not through an excess of neural tissue but through the failure of the neural tube to close and/or the failure of the mesenchyme to develop the cranial roof. There is no evidence of hyperdevelopment of neural tissue to compensate for the loss.

7. Exencephaly is but one gross teratology of the central nervous system which reveals more extensive damage within. It is an extreme condition which must be shared in varying degrees by all members of a litter simultaneously and equally exposed to ionizing radiations.

8. Exencephaly, a major teratology (congenital anomaly) among mammalian fetuses, may be produced by genetic factors after the first generation or by direct exposure of the developing embryos at certain critical stages. In either case the medium of insult is the ionizing radiation; namely, roentgen irradiation. The mechanism, when genetically induced, is no doubt through interference with gastrulation by unbalanced chromosomal complexes, and in the embryo by direct irradiation, due to the high radiosensitivity of the transient neuroblasts. Roentgen irradiation of the embryo produces a phenocopy of the genetically produced exencephaly, for the condition derived in either manner appears to be essentially the same.

9. The period of greatest radiosensitivity with respect to this cerebral congenital anomaly corresponds to 16–18 days for the human embryo.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

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Forty-second Annual Meeting: Caribe Hilton, San Juan, Puerto Rico, March 17–19, 1960.

EDITORIAL

THE FORTY-FIRST ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE American Radium Society completed another successful year of activity when it held its Forty-first Annual Meeting in Hot Springs, Virginia on April 6, 7 and 8, 1959 at The Homestead. The attendance maintained its high level with a total registration of 351, representing 102 members, 127 non-member guests and 122 ladies. Dr. Allen Barker of Roanoke, President-Elect of the Medical Society of Virginia, welcomed the organization to Virginia and expressed the hope that its facilities would be so attractive to the Society that it would return for future meetings.

The Monday morning Scientific Session was opened by Dr. Milford D. Schulz of Boston who delivered the Presidential Address dwelling on "The Choice of Modality in the Treatment of Cancer." President Schulz emphasized that, since this choice was made for the patient's welfare, it should be on the basis of accumulated experience of physicians in various related fields. He also stressed the importance of proper training of the radiotherapist in these times as compared with former years in order to obtain adequate skill and judgment for the best results. The radiotherapist must have an appreciation of the value of surgical and chemotherapeutic methods as well as a thorough knowledge of his own field. He cannot be an all around oncologist on the simple premise that it is difficult to serve more than one master. Time and limitations require sorting out radiotherapy from general radiology. Radium in recent years has been sadly neglected except by the few skilled operators who have used it to advantage in delivering effective radiation to a confined and accessible volume of tissue. Supervoltage therapy should not be based on the mere fact of possession of a high energy unit, but rather on the real uses of this modality. Dr. Schulz was fearful that the value of radiotherapy may be jeopardized by indiscriminate use just because of availability, not tempered by prior experience. He expressed the opinion that the most important development in cancer management is the concept of a team of physicians and scientists, all bringing their own peculiar skills and experience to bear on the patient's problem. Thus, the surgeon, radiotherapist, diagnostician, chemotherapist, physicist, statistician and biologist all set about to do what will serve the situation best and to act in concert.

The morning session continued with a colloquium on "Problems in the Management of Cancer of the Larynx." The moderator was Dr. Ralph M. Caulk and the panel participants were Drs. Leroy Schall and Calvin T. Klopp, representing the surgical point of view, and Doctors Simeon T. Cantril and Robert Robbins, discussing radiation therapy. The indications and contraindications for the various surgical and radiotherapeutic procedures in the management of laryngeal cancer were presented by members of the panel, followed by a thorough discussion relating to morbidity, rehabilitation, physiologic preparation, etiology, management of recurrences, tumor dosage, surgery and radiation failures and many other aspects of the total problem.

The program continued with individual presentations. Dr. Vera M. Dalley of London, England, discussed the place of radiation therapy in the treatment of malignant tumors of the temporal bone. Two other papers completing the morning ses-

sion were on "The Combined Technique of External Irradiation and Interstitial Gamma Therapy in the Treatment of Head and Neck Tumors" and "Cancer of the Nasopharynx." A complete and thorough discussion of the morning presentations was led by Dr. Juan A. del Regato.

In the latter part of the afternoon, Dr. H. Dabney Kerr, in introducing the Janeway Lecturer, recounted in some detail numerous biographical events in the illustrious life of Dr. James T. Case. Dr. Case spoke on the early history of the American Radium Society. He reviewed briefly the events leading to the discovery of radium by Madam Curie and gave many interesting sidelights of her later activities. He told many anecdotes about the exploitations of the public by quacks who offered unusual cures with the use of substances supposedly related to radium. In his tribute to many of the early workers in radium therapy and radiation physics, he especially acknowledged the works of Dr. Gioacchino Failla for his introduction of gold seeds, and Drs. Edith Quimby, J. Ralston Paterson and Herbert M. Parker for placing radium dosage on a scientific basis. Dr. Case reviewed in some detail the various techniques of radium therapy from the very beginning to the present day.

In the early evening, a social hour for members and guests was sponsored by the Radium Chemical Company in the beautiful Georgian Room. After dinner colored movies of Puerto Rico were shown by Dr. Victor A. Marcial, who will be chairman of the committee on arrangements for next year's meeting in San Juan.

The Tuesday morning session continued with a colloquium on the "Causes of Failure in the Treatment of Cancer of the Oral Cavity." Dr. W. S. MacComb was moderator and the panel consisted of Drs. Simeon T. Cantril, Gilbert H. Fletcher, Lewis W. Guiss and Arthur G. James. A lively discussion followed the presentation, and the causes of failure of various modalities used alone and in combination were pointed out. The program continued with presentations on "Roentgen Therapy of Skin and Lip Cancer," "Problems in Planning Radiation Therapy for Postoperative and/or Postradiation Recurrences in Gynecologic Cancer," "The Management of Late Metastases, Recurrences or a Second Primary Tumor in Seminoma," and "Radiation Nephritis and Radiation Myelitis." Dr. Murray M. Copeland of Washington, D. C. summed up the morning program with emphasis on the controversial problems.

On Tuesday evening, following a reception, the Annual Banquet was held in the Georgian Room. After introducing distinguished personalities at the speakers' table, President Schulz, with great eloquence, presented the Janeway Medal to Dr. Case for his outstanding work over a period of many years. The Washington and Lee University Glee Club entertained the group with a fine repertoire of songs. Later, entertainment and dancing followed in the Crystal Room.

The third scientific session took place on Wednesday morning with Dr. Theodore P. Eberhard serving as chairman. This program included the following subjects: "Survival of More Than Ten Years in Hodgkin's Disease," "Marrow Transplant after Exposure to Lethal Radiation," "Psychiatric Problems in Patients Undergoing Radiotherapy," "Common Medical Problems in Patients Undergoing Radiation Therapy," "The Treatment of Retinoblastoma by X-Ray Alone and by the Combination of X-Ray and TEM," "Prognostic Difficulties of Neuroblastoma," "The Moving Strip Technique for Treatment of the Chest Wall following Mastectomy for Cancer of the Breast," "Implantation of Radioisotopes into the Internal Mammary Artery As a Supplement to Radical Mastectomy," "Unusual Radium Implants in the Treatment of Cancer," and "Treatment of Papillomata of the Bladder with Radioactive Colloidal Gold."

During the three morning scientific sessions, a ladies' program was also in progress. This included a lecture by Dean Percy Warren of Madison College, a flower

show by Mrs. Ralph T. Ogden and Mrs. Jesshill Love in the Georgian Room and a coffee hour in the Garden Room.

The substantial scientific contributions, the atmosphere of southern hospitality of The Homestead and superb recreational facilities coupled with the warmth of spring weather contributed in making this meeting unusually successful.

HARRY HAUSER, M.D.

SOCIETY PROCEEDINGS AND NEWS ITEMS

THE ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The next annual meeting of the Rocky Mountain Radiological Society will be held in the Shirley Savoy Hotel in Denver, Colorado, August 20–22, 1959. The guest speakers and their subjects are as follows: Eugene P. Pendergrass, M.D., (1) *Some Intangibles Concerning Cancer;* (2) *Some Thoughts Concerning the Treatment of Inoperable Carcinoma of the Breast;* (3) *Pneumoconiosis;* Philip J. Hodes, M.D., (1) *Altered Cerebral Hemodynamics, Manifestations of Intracranial Disease;* (2) *Rare Pulmonary Diseases, Their Roentgen Manifestations;* (3) *Medical Meddlers, What Price Insecurity;* Franz Buschke, M.D., (1) *The Treatment of Advanced Carcinoma of Head and Neck;* (2) *Common Misconceptions in Radiation Therapy;* Owings W. Kincaid, M.D., (1) *Abdominal Aortography;* (2) *Experiences with Angiography as a Guide to Mediastinal Exploration;* (3) *Roentgenologic Diagnosis of Operable Heart Disease;* and Magnus I. Smedal, M.D., (1) *Therapeutic Uses of Low Megavolt Electrons;* (2) *Observations on the Cause of Arm Edema Following Radical Mastectomy.*

AMERICAN RADIUM SOCIETY ELECTS NEW OFFICERS

At a meeting held at The Homestead, Hot Springs, Virginia, on April 6–8, 1959, the following officers were elected: President, Theodore R. Miller, New York, N. Y.; President-Elect, Jesshill Love, Indianapolis, Ind.; 1st Vice-President, Gray H. Twombly, New York, N. Y.; 2nd Vice-President, Leonidas Marinelli, Lemont, Ill.; Secretary, Robert L. Brown, Atlanta, Ga.; and Treasurer, Gilbert H. Fletcher, Houston, Texas.

The next meeting will be held March 17–19, 1960 at the Caribe Hilton Hotel at San Juan, Puerto Rico.

FOURTH INTERNATIONAL COURSE ON TOMOGRAPHY

The Fourth International Course on Tomography will be held from September 28–October 3, 1959, at the Radiology Institute of the University of Genova, Genova, Italy under the direction of Prof. Alessandro Vallebona. Conferences, lectures, communications have been arranged on various chapters of tomography. All lectures, while read in the original language, will be contemporarily translated into Italian, French, German, and English. The subject "Tomography" will be treated completely in all its aspects: theory, geometric studies, technique and instruments, and its use in exploring several organs in the normal and pathologic individual, with special attention to the more recent procedures and clinical applications.

The entrance fee is 15,000 Italian Lire for ordinary members; 10,000 for junior members (under 30 years of age) and 5,000 for the followers, attendants and relatives. Applications and eventually titles of communications must reach the secretary of the course by June 30. Entrance fees must be sent to the general secretary of the course: Prof. Neopolo Macarini (Istituto di Radiologia, Ospedale S. Martino, Genova), or else be sent to Cook-Wagon-Lits, General Travel agent for this course. Applicants may ask the same agencies for information concerning their travel and hotel bookings.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Neck and Chest

Hafter, Ernst. Hiatal hernia; its diagnosis and clinical significance. *Am. J. Digest. Dis.*, Dec., 1958, *3*, 901–915. (Address: 36 Toedistrasse, Zürich, Switzerland.)

Hiatal hernia is no longer a rare finding. It is often overlooked because, even though the symptoms are quite characteristic, they are not generally known and the diagnosis which is a roentgenologic one is not always adequate.

There are no problems to diagnosis of large hernias; it is the small spontaneously reducible ones which produce the severest symptoms.

The author gives several criteria for good diagnosis. The lower end of the esophagus and the cardia must be filled with opaque mixture. The patient must be horizontal and exposure made on expiration. Another maneuver is increasing intra-abdominal pressure.

Roentgenograms are recommended in the following postures: prone with left side elevated (here small hernias may be overlooked), prone with epigastric pressure made by pillow, sponge or balloon (this is most reliable), and left oblique supine in Trendelenburg position (not too reliable).

If indirect signs of hernia are encountered, all efforts should be made to prove its presence, even using air in the colon and the Valsalva maneuver. The indirect signs are: passage of barium into the stomach during inspiration (normally the pinchcock action of the hiatus shuts off the lower end of the esophagus on deep inspiration); reflux into the esophagus in Trendelenburg position; and irregularity of the mucosal pattern of the lower esophagus or S-shaped tortuosity which may be an incompletely filled hernia.

The author performed 2,402 barium meal examinations and found a 12.5 per cent incidence of hernias in patients with epigastric complaints. However, he feels that in nonselected cases this would be 8–10 per cent. The most common age group is past fifty years, although congenital hernias can occur.

The symptoms are those due to: (1) incompetence of cardia—causing fullness, substernal discomfort, pressure in left chest; (2) regurgitation into the esophagus—causing burning, bitter eructations; and (3) posture—causing symptoms to be worse in the recumbent position or when bending over.

An interesting observation in the author's series was that Saint's triad (hiatal hernia, gallstones, diverticulosis of the colon) was seen in 2.3 per cent of his cases. There are 9 fine illustrations and 3 tables showing correlation of size of hernia, age and symptoms.—*Eva S. Carey, M.D.*

Béraud, Cl., and Deffrenne, P. Étude radiologique des hernies par aplasies diaphragmatiques partielles du nouveau-né. (Radiologic study of hernias due to partial diaphragmatic aplasia in the newborn.) *J. de. radiol., d'électrol. et de méd. nucléaire*, Nov., 1958, *39*, 697–704. (Address: Cl. Béraud, Chemin Sainte-Irénée, Lyon, France.)

The authors report 5 cases operated on for congenital hernias in the newborn due to partial aplasia of the diaphragm; of these, 4 were on the left and 1 on the right side. These malformations, sometimes immediately fatal, scarcely permit survival beyond a year. They result from the persistence of the posterior pleuroperitoneal sulcus, and the viscera enter the thorax through the foramen of Bochdaleck, producing grave cardiorespiratory changes—dyspnea, cyanosis, and dextrocardia. The diagnosis, which should be made as soon as possible, is based on the roentgenologic examination. Plain films will show identifiable gas patterns in the left base or an opacity caused by the liver in the right hemithorax, while contrast studies made with lipiodol will show normal placement of the stomach and the presence of intestinal loops in the thorax. Laminagrams demonstrate displacement of the lung and are particularly useful in right-sided hernias. Barium enema studies are of value in outlining the anterior hernias through the foramen of Larrey. The clinical findings and roentgenologic signs suffice to identify the hernias easily and to differentiate them from eventrations, diaphragmatic paralysis, air-filled cysts and bullous emphysema of the left base.

Modern operative technique permits the salvage of 8 out of 10 of these newborns.—*Frank A. Riebel, M.D.*

Podesta, Horacio, and Arla, Julio Ernesto. Miositis primaria del diafragma; síndrome de Hedblom. (Primary myositis of the diaphragm; Hedblom's syndrome.) *Prensa méd. argent.*, May 23, 1958, *45*, 2024–2028. (Address: V. López 1857, Buenos Aires, Argentina.)

An inflammation of the diaphragm may cause elevation and immobility in the absence of obvious abdominal, mediastinal, pleural, or pulmonary lesions or of lesions of the phrenic nerve. The symptom is pain around the costal margin, which at times may be referred to the shoulder.

The pathologic changes in the diaphragm indicate an exudative and proliferative type of inflammation. Muscular fibers are replaced by fibrous tissue, after which flattening of the diaphragm, elevation, and immobility occur.

The therapy is asymptomatic, antibiotics being indicated for secondary infection.—*Charles M. Nice, Jr., M.D.*

Abdomen

Schatzki, Stefan C., and Blade, William R. Emergency x-ray examination in the diagnosis of severe upper gastrointestinal bleeding. *New England J. Med.*, Nov. 6, 1958, *259*, 910–912. (From: The Department of Radiology, Massachusetts General Hospital, Boston, Mass.)

The authors review an unselected series of acute, massive upper gastrointestinal bleeders including 108 patients.

The best chance for definitive diagnosis is within the first thirty-six hours after the onset of bleeding. Three out of 4 cases were given specific diagnoses. In half of the cases not diagnosed within the first thirty-six hours, the bleeding point was not found during the hospitalization. The technique of examination is not discussed but the standard references are given. The authors believe that, after the patient is out of shock, the stomach should be aspirated of all possible blood and secretions and that the gastric tube should be removed before the examination.

The authors conclude that delay in examination of an acute bleeder may interfere with the management of the patient, may lead to blind exploration and may result in a not more but rather less accurate diagnosis as compared with the early examination.—*Martin A. Thomas, M.D.*

Johnson, George F., and Wright, Orville. Eosinophilic infiltration of the stomach. *Radiology*, Sept., 1958, *71*, 415–419. (Address: 2197 Los Arrow Drive, Dayton 9, Ohio.)

The authors present a case of eosinophilic infiltration of the stomach along with a review of the literature. This probably represents the first such case reported in which a provisional diagnosis was made roentgenographically and subsequently confirmed by surgical excision and pathologic examination.

The patient, a fifty-three year old married white woman, was first seen with a two week history of postprandial epigastric pain associated with occasional vomiting. She was known to be sensitive to sulfa drugs and, for the prior two months, she had been experiencing asthmatic attacks. The physical examination was within normal limits except for a right upper quadrant incisional hernia, occasional irregular cardiac ventricular contractions, and wheezing type of respiration. The initial blood cell count revealed an eosinophilia of 54 per cent and after being repeated of 45 per cent. An upper gastrointestinal study demonstrated slight gastric dilatation, no apparent peristalsis, and delayed gastric emptying. This study was repeated two days later with the findings of slightly more gastric dilatation, no visible peristalsis, and no delay in gastric emptying. The small bowel loops were noted to be slightly dilated.

In view of the roentgenologic findings and the eosinophila the radiologist suggested infiltrative eosinophilic gastritis and enteritis as the most likely possibility. The patient subsequently was subjected to abdominal exploration, at which time 2,000 cc. of straw-colored fluid was found in the peritoneal cavity. Due to the presence of thickening and a questionable mass involving the distal end of the stomach a subtotal gastric resection was performed. Microscopic examination of the specimen revealed a thick pyloric wall and antrum and marked eosinophilic infiltration of all layers of the stomach including the mucosa and serosa. The patient's convalescence was uneventful. A follow-up blood cell count on the eighth postoperative day disclosed a residual eosinophilia of 16 per cent.

This case and the other recorded cases of diffuse eosinophilic infiltration of the stomach seem to be entirely separate from the localized eosinophilic tumefactions as originally described by Vanek wherein the patients have no allergic history and no eosinophilia. The case reported here lends support to the basic supposition that the eosinophilic infiltration is an additional manifestation of an allergic condition. The authors suggest that, in the situation of an adult with eosinophilia and epigastric distress, the following roentgenologic findings may be diagnostic of diffuse gastric eosinophilic infiltration: (1) initial fluid retention with mild to moderate gastric dilatation; (2) little or no gastric peristalsis; and (3) gastric emptying within three to four hours despite peristaltic alteration. The presence of abdominal fluid and small bowel dilatation with an altered mucosal pattern may be additional diagnostic evidence.—*Edward B. Best, M.D.*

Ravitch, Mark M. Intussusception in infancy and childhood; an analysis of seventy-seven cases treated by barium enema. *New England J. Med.*, Nov. 27, 1958, *259*, 1058–1064. (From: The Department of Surgery, Johns Hopkins University and Hospital, and Baltimore City Hospitals, Baltimore, Md.)

The value of reduction of intussusception by barium enema was proven in a series of 77 cases. In this series 69 per cent were relieved by barium enema alone. In 5 cases operation was done to merely confirm the fact of complete reduction, so actually 75 per cent is a more accurate figure.

The importance of early diagnosis is stressed. The fatalities were directly proportional to delay or error in diagnosis.

The procedure is carried out with the operating room in readiness. The barium canister is raised no higher than $3\frac{1}{2}$ feet from the table top and no manual pressure is used. The buttocks are strapped together and a balloon obturator employed. If the reduction

is not completed and no progress is made in moving the opaque column after ten to fifteen minutes, the attempt should be abandoned and operation proceeded with. However, if only a little progress, no matter how slowly, is made, the attempt should be persisted in. It is important also, that a large portion of the small bowel be filled to insure complete reduction.

The causes found for intussusception in this series were: Meckel's diverticulum (5 cases); large lymphoid patch (1 case); polyps (5 cases); and ectopic pancreatic tissue (1 case).

It is stressed that a barium enema reduction of intussusception is a surgical procedure performed by surgeons while the operating room is held in readiness. Gangrenous bowel will not be reduced and perforation of the intestine will not occur if the canister is kept $3\frac{1}{2}$ feet above the table top and no manual pressure is exerted.—*Eva S. Carey, M.D.*

Traissac, F.-J., Leger, H., Dabadie, J., and Sehabiague, L. (Bordeaux, France.) Carcinoïde du grêle avec métastases hépatiques et rétrécissement pulmonaire. (Carcinoid of the small intestine with hepatic metastases and pulmonary stenosis.) *Arch. mal. app. digest.*, Oct., 1958, *47*, 1082–1094.

The authors report a case of carcinoid of the small intestine associated with a progressive development of pulmonary stenosis.

This fifty-two year old woman also showed the classic phenomenon of "flush" hepatic metastases, and excessive serotin (130 mg. of 5 hydroxytrybtamine in the urine every twenty-four hours).

In a period of eight months the patient was operated on twice and, contrary to expectation, it was found that the hepatic metastases had diminished in number.

At the second operation, after excision of the main tumor, the 5 hydroxytrybtamine content of the urine had not decreased but had increased to 165 mg. per twenty-four hours, thus proving the essential part played by the hepatic metastases in the hypersecretion of serotin. This increased serotin seems to have a determining role in producing the right sided cardiopathy.—*Maurice Dufresne, M.D.*

Maria Giussani, Ricardo, and Pozo, Osvaldo O. Sarcoma reticulocelular del ileon terminal. (Reticulum cell sarcoma of the terminal ileum.) *Prensa méd. argent.*, March 21, 1958, *45*, 1254–1264. (Address: Pozos 175, Buenos Aires, Argentina.)

Tumors of the small bowel are often missed because of the difficulty in visualizing them on roentgenologic examination. When a patient shows anemia, weight loss, melena, and vague gastrointestinal symptoms, it behooves the internist to insist that every possible technique of roentgenologic examination be used to try to establish the diagnosis.

One case of reticulum cell sarcoma of the ileum is reported. The diagnosis was finally made when the tumor was visualized by means of a small-bowel enema, which had been preceded by three negative upper gastrointestinal series and a conventional barium enema study.—*F. Comas, M.D.*

Chucker, George N., and Gilmer, Wm. P. Preparation of the colon prior to barium enema. *Radiology*, Oct., 1958, *71*, 570–572. (Address: G. N. Chucker, Chesapeake and Ohio Railway Hospital, Clifton Forge, Va.)

Proper preparation of the colon prior to barium enema examination is of utmost importance, first of all to make adequate diagnosis possible, and secondly to avoid the added radiation incident to repeat examination. The authors suggest the following procedure:

I. The day prior to examination:
   (a) A clear liquid diet or, if this is not feasible, at least a liquid supper.
   (b) Two ounces of castor oil at 4–6 p.m.
   (c) Nothing by mouth after midnight, juices permissible up to that time.

II. The day of examination:
   (a) Omit all fluids or food prior to the examination.
   (b) At 6 a.m., two soap suds enemas (800–1,000 cc.). Half of each enema is given with the patient lying first on his left side, then on the right side.
   (c) Following the above, 1,000 cc. of warm water containing three-quarters to one teaspoon of tannic acid is instilled. (The authors found that the 1 per cent solution used by others caused too much irritation and cramping. They recommend this weaker solution.)
   (d) Follow with a plain water enema (1,000 cc.).
   (e) After completion of the examination, the patient is returned to his room and a soap suds enema is given to remove the remaining barium.

It is the authors' belief that patients prepared in this way also allow excellent studies of the lumbosacral spine, pelvis, intravenous pyelograms and cholecystograms with very little disturbance from overlying gaseous shadows.—*Z. Petrany, M.D.*

Creevey, Kennedy, Cohen, Jerome L., and Riley, George J. Pneumatosis of the descending colon. *New England J. Med.*, Nov. 6, 1958, *259*, 912–915. (From: The Departments of Surgery and Medicine, Samaritan Hospital, Troy, N. Y.)

The authors report a case of pneumatosis of the colon in a fifty-three year old female localized to a 20 cm. area of the descending colon. The patient complained of abdominal gas and alternating diarrhea and constipation of three months' duration. The barium enema study showed a loss of normal mucosal markings in the involved area with scalloping of the borders and compression of the lumen. The involved area was resected. The patient has remained in good general health but continues to have intermittent colicky pains with slight irregularity of bowel function.

The etiology of the condition is unknown. The mechanical theory that gas is forced through a break in the mucosa is satisfactory for some cases. However, the majority of the cases reported by Koss in 1952 involved the small intestine and were associated with peptic ulcer and obstruction of the stomach. Sigmoidoscopy has been implicated in some cases as a possible cause.

Diagnosis may be made by noting clusters of air density on the survey roentgenogram of the abdomen. Barium enema and upper gastrointestinal studies aid in confirming the diagnosis and localizing the involved bowel.

Generally, pneumatosis is a benign condition secondary in nature. Treatment is that of the primary cause. Surgery is not recommended when the condition is diagnosed prior to laparotomy. When a localized lesion is unexpectedly encountered at surgery, the authors believe resection advisable.—*Martin A. Thomas, M.D.*

Feinberg, S. B., and Lester, R. G. Roentgen examination of the gastrointestinal tract as an aid in the diagnosis of acute and subacute reticuloendotheliosis. *Radiology*, Oct., 1958, *71*, 525–533. (Address: S. B. Feinberg, 737 E. 22nd St., Minneapolis 4, Minn.)

The authors describe a previously unrecognized roentgen finding in the gastrointestinal tract of patients with reticuloendotheliosis. This consists of an abnormal mucosal pattern and altered motility of the small bowel.

Two cases of reticuloendotheliosis with their gastrointestinal findings are reported. One patient, a nine-month old male infant with acute reticuloendotheliosis, was examined because of vomiting and distention. The barium study revealed an abnormal mucosal pattern of the duodenum and jejunum which varied from complete effacement in some areas to a coarsened and granular, somewhat pebble-like appearance in other areas. The distal ileum presented some segmentation and flocculation, with less striking mucosal alteration. A postmortem examination revealed a thick small bowel wall due to reticuloendothelial mononuclear cell invasion. The second patient, a three-year old female with subacute reticuloendotheliosis, was recalled as a result of the above study and similarly examined. She was found to have a coarse mucosal pattern in the jejunum and ileum and definite segmentation of barium in the distal small bowel. Subsequent study of the University of Minnesota files from 1932 through 1957 disclosed 22 proved cases of reticuloendotheliosis, of which 11 were acute forms of the disease. Seven of the 11 acute cases were found at autopsy to have intestinal and /or mesenteric lymph node involvement and 6 of the 7 had exhibited gastrointestinal symptoms of either vomiting, distention or diarrhea. From the above findings the conclusion was reached that the acute reticuloendothelioses are more likely to present gastrointestinal symptomatology.

Obviously a gastrointestinal examination is not indicated in cases with the typical or classical findings of reticuloendotheliosis. However, a routine barium examination is advocated in all instances of vomiting and diarrhea since these may be the only clinical symptoms in atypical reticuloendotheliosis. In such instances, the recognition of abnormal motility and mucosal patterns, as described, could give the initial clue leading to the performance of accepted laboratory procedures for a final diagnosis.—*Edward B. Best, M.D.*

Culver, Gordon J., Pereira, Rubens Marcondes, and Seibel, Roy. Radiographic features of rectosigmoid endometriosis. *Am. J. Obst. & Gynec.*, Dec., 1958, *76*, 1176–1184. (From: The University of Buffalo School of Medicine, Buffalo General Hospital, and Buffalo Deaconess Hospital, Buffalo, N. Y.)

The condition referred to as endometriosis is not uncommon in gynecologic practice. Through several routes, endometrium can invade or become implanted upon practically every pelvic organ and more rarely upon extrapelvic organs.

Benign endometrial cells are capable of dissemination and metastasis along the same pathways followed by endometrial adenocarcinoma. By direct extension or by lymphatic spread to adjacent serosal surfaces, the endometrial cells can become implanted upon the intestines. Because of their close proximity, the rectum and rectosigmoid colon are the most frequently involved segments (70 to 80 per cent of the reported cases). However, many cases of involvement of the small intestine and of the appendix have also been reported.

The roentgen-ray findings of rectosigmoid endometriosis by barium enema can be classified into 2 groups: constricting and nonconstricting lesions. Implants on portions of the bowel which are freely suspended by a mesentery are less likely to become constricting lesions than are implants upon portions of the bowel which are partially extraperitoneal and more firmly attached.

In constricting lesions the following roentgenographic changes are noted: Annular narrowing of

variable length, usually relatively short, with or without an associated filling defect caused by the endometrial tumor. Most frequently the narrowing tends to be eccentric. The area of involvement is sharply demarcated. The lesions are usually fixed and tender when palpated under fluoroscopic observation. Most important is the fact that the mucosal folds are intact through the lesions.

In nonconstricting endometriosis the findings are different. A submucosal tumor is demonstrated with normal mucosa overlying and surrounding the lesion. The extraluminal extent of the lesion may produce varying degrees of displacement of the bowel. A localized spastic and irritable segment of bowel is seen above and below the lesion.

Seven cases and 8 good illustrations make this an excellent article to read in full.—*Eugene J. McDonald, M.D.*

ANTONIAZZI, BRUNO. Le metastasi gastrointestinali da carcinomi dell'utero. (Gastrointestinal metastases from carcinoma of the uterus.) *Radiol. med.*, Nov., 1958, *44*, 1043–1049. (From: Istituto di Radiologia della Università, Milano, Italy.)

The author has reviewed the literature and affirms that the various investigators have noted that metastasis from carcinoma of the uterus via the vascular channels is indeed a rare occurrence. It is only slightly more frequent in malignancy of the cervical portion of the uterus.

A summary of the lymphatic and venous pathways indicates that the course of the metastases is eventually through the superior and inferior venae cavae through the heart to the pulmonary circulation. The ultimate destinations are principally the lungs, the brain and the skeleton. There is also the possibility of metastases through the portal system. This may occur in two ways: (1) by extension to the peritoneum, thence through the venous flow of the portal and inferior caval systems; and (2) by the known direct anastomoses between the portal and inferior caval systems.

The author presents 2 cases of metastases from carcinoma of the uterus, one to the proximal portion of the transverse colon and the other to the pyloric antrum, which are considered in the light of the previous discussion.—*Anthony A. Blasi, M.D.*

ROSE, J. DUDFIELD. Serial cholecystography; a means of preoperative diagnosis of biliary dyskinesia. *A.M.A. Arch. Surg.*, Jan., 1959, *78*, 56–66. (Address: 35 Eslington Terrace, Tyne 2, England.)

Biliary dyskinesia may be defined as a disorder of the motility of the biliary tract. The author feels that it is a frequent occurrence. Serial cholecystography gives the patient minimum discomfort and is the method of choice in the majority of cases for the investigation of this condition.

Fourteen hours after a single dose of iopanoic acid (telepaque) anteroposterior and lateral roentgenograms of the gallbladder region are made with the patient supine. If the gallbladder is not seen clearly or if gallstones are present, the examination is discontinued. If the gallbladder is opacified, the patient is given 100 cc. of ice-cold isotonic saline to drink and is kept in the prone position for five minutes. Then a standard fatty meal is administered and the patient is turned into the supine position. Anteroposterior and lateral roentgenograms are subsequently made at ten, twenty, thirty and eighty minutes after the fatty meal. Subsequently the gallbladder shadows are traced and the volume computed. The angle between the long axis of the gallbladder and the long axis of the spine in the lateral view, the angle of erection, is also measured.

The study of the evacuation curve in conjunction with the curve of the angles of erection is the most important factor in making a diagnosis of functional abnormalities of the biliary tract. With moderate insufficiency of evacuation there may be vesicular hypertonia in such condition as cystic duct obstruction or infundibulocystic kinking. The initial volume of the gallbladder may be greater than normal in cases of spasm of the sphincter of Oddi or other common duct obstructions. On the other hand, insufficiency of evacuation may be associated with vesicular hypotonia. When a gallbladder evacuates very rapidly there may be hypertonia such as in functional dyskinesia with parasympathetic predominance or it may be secondary to neighboring inflammatory lesions such as duodenitis or ulcer. Rapid emptying can also be associated with hypotonia when there is loss of tone of the sphincter of Oddi.

It is felt that biliary dyskinesia is present in more than two-thirds of patients who come to consultation with what might be called symptoms of biliary-tract disorder. Serial cholecystography is a much more accurate method of diagnosis in these cases than is clinical examination alone or "classical" cholecystography.—*Arthur E. Childe, M.D.*

JUTRAS, ALBERT, LONGTIN, MARCEL, and LÉVESQUE, HENRI-PAUL. La cholestérolose et ses manifestations radiologiques. (Cholesterolosis and its radiologic manifestations.) *Ann. de Radiol.*, 1958, *1*, 179–210. (From: Départments de Radiologie de l'Hôtel-Dieu de Montréal et de l'Université de Montréal, Montréal, Canada.)

Cholesterolosis, also referred to as strawberry gallbladder, is a pathologic condition characterized by the deposition of certain lipoid substances on the inner aspect of the gallbladder wall within the mucosa. This condition of relatively frequent occurrence is well known to pathologists but has been the

subject of little interest, if any, to the clinician and the radiologist.

The authors stress the histopathologic findings as a basis for understanding and interpreting the roentgenologic manifestations.

Cholesterolosis may be classified into two types: (1) diffuse, micronodular, or so-called strawberry gallbladder (the latter term is not considered truly applicable and is not recommended). In this type cholesterol deposits are within and on the epithelium of the gallbladder wall, appearing as round or elongated granules. This results in irregular serrations of the silhouette or contour of the gallbladder when filled with the contrast medium; and (2) localized or polypoid. In this type, the cholesterol deposits involve a limited area of the gallbladder mucosa which is sharply defined. This may be solitary or multiple, sessile or more or less pedunculated. The lesions present fixed, well defined filling defects on the roentgenogram, particularly in the tangential projections. They are frequently multiple and may occur at any level of the inner wall of the gallbladder. The size of each lesion does not exceed 1 cm., and is usually 0.5 cm. or less. Solitary lesions tend to occur in the mid-third while multiple lesions may be distributed throughout.

It is not possible to determine from the roentgenologic appearance the true type or histology of a lesion. Differential diagnosis includes a true papilloma (considered neoplastic, benign, though potentially malignant) or an inflammatory adenoma. Not infrequently neuromatosis is observed within the mucosa, often associated with cholesterolosis. This condition is referred to as neurolipoidosis.

The authors stress the importance of using the term polyp to designate all filling defects, be they single or multiple. The term papilloma or adenoma should be reserved for the distinctive types of lesions which are neoplastic or inflammatory, respectively.

Improvement in technique and better contrast media have helped in improving the diagnosis. Once suspected, the polypoid lesion can be confirmed by repetition of the examination as well as by the use of compression spot roentgenograms. A high index of suspicion should be maintained. While increased density of the contrast medium may obscure the tumor, in the filled gallbladder better delineation occurs with sharper definition of the tumor. Delayed roentgenograms with greater emptying often reveal the presence of several defects in addition to the one originally suspected.

The indirect roentgen signs are: (1) excessive or high concentration of the contents of the gallbladder due to increased absorption through an increased mucosal surface; (2) hyperkinesia or rapid and early emptying in quick response to the stimulus of a fat meal. The degree of thrust of the emptying of the bile into the upper gastrointestinal tract may be accompanied by spontaneous pain and disgestive discomfort. The authors believe that hyperkinesia, in part, is due to increased nerve tissue element proliferation, with the association of neuromatosis and cholesterolosis, so-called neurolipoidosis.

In a series of 609 oral cholecystographies, 46 patients had cholesterolosis: 41 or 86 per cent had shadows of normal or above normal density; 4 had shadows below normal density and in 1 the gallbladder did not visualize because of a calculus impacted at the gallbladder neck.

Six tables, 26 beautiful reproductions of roentgenograms and photomicrographs, and 4 colored plates of anatomic specimens accompany this excellent and comprehensive article.—*William H. Shehadi, M.D.*

Lepennetier, F., Picard, J. M., and Hernandez, Cl. (Paris, France.) Calculus vésiculaires flottants et mégacystique calculeux. (Floating gallstones and stone in dilated cystic duct.) *J. de radiol., d'électrol. et de méd. nucléaire*, Nov., 1958, *39*, 742–745.

The authors' case showed floating gallstones in addition to a giant cystic duct dilatation resulting from a partly obstructing calculus. Usually when the gallbladder is visualized by means of oral contrast media, as in this instance, the dependent bile is the denser, the supernatant bile is less opaque and a clear zone between them represents calculi. Quoting Pelissier *et al.*, however, the authors point out that calculi can be erroneously diagnosed when the study is made with intravenously administered contrast media. If roentgenograms are taken in the erect position, the supernatant fluid is more opaque since its source is the liver; transiently, some of this iodized bile may flow down along the wall of the gallbladder and may opacify the fundus as well, leaving an intermediate clear zone.—*Frank A. Riebel, M.D.*

Lasala, Atilio J., and Saporta, José Alberto. Fistulas biliodigestivas espontaneas; nuestra experiencia con 51 casos. (Spontaneous bilidigestive fistulas; experience with 51 cases.) *Rev. Brasil. de gastroenterol.*, June–Aug., 1958, *10*, 147–156. (Address: Dr. A. J. Lasala e Col, Buenos Aires, Argentina.)

Spontaneous bilidigestive fistulas occur most frequently between the gallbladder and duodenum, but are also seen communicating with the stomach and colon. At times, the surgeon may find such a fistula when operating upon a patient who has an intense pericholecystitis. Apparently most of these fistulas originate in the gallbladder, sometimes perhaps caused by simple erosion due to gallstones, at other times by inflammations, either in the gallbladder or in the surrounding tissues.

The presence of air in the biliary tree on roentgenographic examination is a very suspicious finding

unless the patient has had a previous sphincterotomy at the sphincter of Oddi. Also, barium may be seen filling a fistula following barium meal or barium enema studies. Although not specifically mentioned in this paper, occasionally, carcinomas, such as in the proximal portion of the transverse colon, may be the starting point of a fistula between the gallbladder and the colon. Another type of fistula is sometimes caused by an erosion of the stone through the distal portion of the common duct into the nearby duodenum, thereby creating a definite fistulous tract.—*Charles M. Nice, Jr., M.D.*

CIMMINO, CHRISTIAN V. Carcinoma in a well-functioning gallbladder. *Radiology*, Oct., 1958, *71*, 563–564. (Address: Mary Washington Hospital, Fredericksburg, Va.)

The author reports a case of carcinoma of the gallbladder with excellent concentration of the contrast medium. A constant filling defect measuring 5×10 mm., which was fixed to the medial wall of the gallbladder, was seen in the contrast medium. Study of the surgical specimen disclosed that this was a frank "papillary adenocarcinoma, non-invasive."

Noncalculous filling defects within the gallbladder can be divided as follows: (1) metabolic—which are usually small and multiple; (2) inflammatory—usually occurring in a gallbladder with poor concentrating power; (3) neoplastic—usually a single lesion; and (4) malformations. No accurate criteria are available for accurate differential diagnosis of these noncalculous defects. For this reason, the author feels that all such filling defects constitute an adequate indication for surgical exploration lest a malignant or potentially malignant lesion be missed. —*Arno W. Sommer, M.D.*

FRANK, A. Über den Wert des Schichtverfahrens bei der Cholangio-Cholezystography. (The value of laminagraphy in cholecystocholangiography.) *Radiologia Austriaca*, 1958, *10*, No. 1, 41–47. (From: Zentralröntgeninstitut der Krankenanstalt Rudolfstiftung, Boerhavegasse 8, Wien III, Austria.)

The author examined the biliary system with laminagraphic procedures in 240 patients. Routine gallbladder examinations with intravenous biligrafin may give poor contrast in heavy patients; in addition, overlying intestinal gas may cause confusing shadows. This is expecially true when biligrafin is used for visualization of the biliary duct system. The fact that the hepatic, cystic, and common duct lie in one level is the anatomic basis for laminagraphic studies of the biliary system. This examination is less helpful in demonstrating the gallbladder, since this organ occupies an oblique position.

It has been found that 40 cc. of intravenously injected 30 per cent biligrafin gives better visualization of the biliary ducts than 20 cc. of 50 per cent biligrafin. This is probably because a larger dose of the less concentrated contrast material results in a more protracted excretion. Fifty minutes after the injection, the patient is placed in the supine position with his right side elevated 20 to 30 degrees. Laminagrams are taken at a depth of 6, 7, and 8 cm. or of 7, 8, and 9 cm. Three laminagrams usually suffice. The rountine cholecystograms are taken two hours after the injection.

By using the above procedure the diagnostic accuracy was improved in 5 per cent of the patients, especially in those with stones in the ducts. The author reports several cases (proven by illustrations) in which a stone could not be identified on the routine gallbladder examination with biligrafin, whereas the laminagram demonstrated the calculus very clearly.

The author prefers the laminagraphic examination of the biliary system to operative cholangiography. It is important, however, that this diagnostic procedure be done shortly before surgery.

This examination may also prove helpful in the future for the diagnosis of tumors of the biliary system.—*Wolfgang H. Steinmetz, M.D.*

SEVERIN, G., and FRANZEN, J. Baygnostil, ein neues trijodiertes orales Gallenkontrastmittel. (Baygnostil, a new triiodide oral gallbladder contrast medium.) *Chirurg*, Dec. 1958, *12*, 550–552. (From: Röntgen- und Strahleninstitut der Johannes Gutenberg-Universität, Mainz, Germany.)

The authors report the use of a new oral gallbladder contrast medium, baygnostil (Bayer), on 400 patients ranging from sixteen to seventy-six years of age. It is the 2, 4, 6-triiodo alpha butyric acid with 68.2 per cent iodine content by weight. It has a very low toxicity and the LD_{50} for mice is 5.0/kg. for oral administration. No vomiting, diarrhea or flatulence was observed and only occasionally a disturbing residual contrast substance remained in the intestines.

The image density is much superior to that obtained with bivalent iodine preparations, although this is not advantageous in every case, as small concretions may be overshadowed with too much contrast. On the other hand, the high iodine content may produce visualization of the gallbladder with less concentration or when the patient is obese.

The authors did not find the intravenous cholangiogram to be much superior to the oral cholangiogram by baygnostil in the visualization of the gallbladder.

The method of examination is as follows: twelve to sixteen hours after the oral administration of 3 gm. of baygnostil in 6 tablets, a survey Bucky roentgenogram is made in the oblique projection. This is

followed with spot roentgenograms under fluoroscopic control in various projections in the prone and erect postures. A final examination is made approximately forty-five minutes after a fatty meal. Often the bile ducts are visualized twenty to thirty minutes after a fatty meal with a good gallbladder response. It is important, however, in these cases to make stereoscopic roentgenograms in two planes, taking the topographic-anatomic relations into consideration.—*Salomon Silvera, M.D.*

Jones, Malcolm D., Sakai, Hsajiq, and Rogerson, Alexander G. Intravenous cholangiography in children with fibrocystic disease of the pancreas; a pilot study. *J. Pediat.*, Aug., 1958, *53*, 172–179. (From: The Departments of Radiology and Pediatrics, University of California, School of Medicine, San Francisco, Calif.)

This investigation was undertaken in an attempt to study the biliary ducts and detect abnormalities which might possibly be associated with fibrocystic disease of the pancreas.

Seventeen children were examined with an age range between nineteen months and eleven years. The diagnosis was made on the basis of clinical findings, roentgenograms of the chest and the lack or depression of pancreatic enzymes. One of these patients was subsequently reclassified as normal and was used as a control. All underwent the usual therapy.

The method of examination with the usual prestudy routine was carried out and then 1.0 cc. per 2 kg. of weight of cholografin was injected intravenously up to a maximum of 20 cc. This was done over a ten minute period. Preinjection roentgenograms were made, followed by conventional roentgenograms and laminagrams after injection. The patients were kept supine and on occasion stereoscopic roentgenograms were also made.

Of interest was the rapid appearance of the contrast medium in the biliary ducts which was often noted within two minutes following completion of the injection. The laminagrams were valuable in many instances. The visualization of the bilary ducts was good in approximately half of the patients and fair to poor in the rest. Most exhibited some collection of the cholografin in the gallbladder, while 7 of the 16 showed poor urinary excretion. The intrahepatic ducts were described as broad in 7 and narrow in 6 patients. It seemed that the younger the patient when the disease was diagnosed the more frequently the broad pattern of the ducts occurred.

The use of intravenous cholangiography in patients with fibrocystic disease of the pancreas does not seem to lend itself to any particularly prognostic or diagnostic conclusions.—*John L. Gwinn, M.D.*

Hepp, Jacques, and Moreaux, Jean. (Paris, France.) Documents sur les pancréatites avec calcifications. (Pancreatitis with calcifications.) *Arch. mal. app. digest.*, Oct., 1958, *47*, 1057–1072.

Valuable observations on pancreatitis with calcification were made on 13 patients subjected to surgery. Young men seem to be mostly affected. This disorder is apparently independent of biliary lithiasis and in 9 of the 13 cases it coincides with chronic alcoholism. The surgical indication is based on the violence of the pain syndrome. Roentgenographic findings of calcification enable a precise diagnosis to be made. The presence of a total or localized portal hypertension, as well as the effect in the main biliary tract, are essential factors in determining the surgical procedure.

There are three types of pancreatic lesions: (1) atrophic; (2) hypertrophic with distention of the canal; and (3) cavitary with a pseudocyst.

Pancreatography allows a detailed study of the duct of Wirsung and influences the choice of a pancreatic operation. Of the 13 patients, 11 underwent a pancreatic operation and 12 a biliary operation.

The results are discussed and attention drawn to the later possible occurrence of diabetes.—*Maurice Dufresne, M.D.*

Balestra, Edmondo. Sulle distopie spleniche; (con particolare riguardo ai rapporti di milze ectopiche con lo stomaco ed all'interposizione gastro-diaframmatica della milza). (On splenic ectopia [with particular attention to the relationship of the stomach to the ectopic spleen and to gastrodiaphragmatic interposition of the spleen].) *Radiol. med.*, Nov., 1958, *44*, 1025–1043. (From: Istituto di Radiologia dell'Università, Genova, Italy.)

Splenic ectopia may be caused by: (1) congenital factors, principally, development in an anomalous site and laxity of ligaments; and (2) acquired factors, namely, hypertrophy, perisplenitis, and changes in intra-abdominal pressure.

Symptomatology may be lacking or atypical, particularly in compression of the greater curvature of the stomach. In cases of gastrodiaphragmatic interposition, symptoms prevail because of irritation of the fundus of the stomach and interference with cardiac function.

The author describes 13 of his own cases. In one, the spleen which was congenitally ectopic and deformed, although of a normal volume, compressed the greater curvature of the stomach simulating a neoplasm. In the other cases, the spleen was interposed between the stomach and the diaphragm. In two of these, a carcinoma of respectively the fundus and the body of the stomach was also present.

An interesting case is reported in which there was a postoperative eventration of the diaphragm with a

protrusion of the spleen into the thoracic cavity simulating a diaphragmatic herniation.—*Peter P. Brancucci, M.D.*

GYNECOLOGY AND OBSTETRICS

GRABER, EDWARD A., BARBER, R. K., and O'ROURKE, JAMES J. X-ray pelvimetry. *Am. J. Obst. & Gynec.*, Jan., 1958, *77*, 28–33. (From: Obstetrical Services of Lenox Hill Hospital and St. Clare's Hospital, New York, N. Y.)

The authors have reviewed 242 cases of roentgen-ray pelvimetry reported by 18 different radiologists. The prognostic accuracy was correct in 3 out of 4 cases but the degree of error was much higher in borderline situations where the obstetrician needed the most help. The greatest percentage of error resulted from the inability of the roentgenologist to judge the size of the fetal head, regardless of the method used.

Roentgen-ray pelvimetry is a laboratory adjunct to the physician's clinical judgment. The roentgenologist usually has no intimate knowledge of the clinical mechanisms of the various presentations and positions, the patient's parity and age, the condition of her soft tissues, her emotional stability, the strength and character of her uterine contractions and her progress during labor. He should report what he sees but the outcome of delivery should not be expected as a part of his evaluation. The obstetrician should not be intimidated by the roentgenogram, for an adequate trial of labor is still the best way of testing pelvic capacity.

The usual indications for pelvimetry are too broad and should be changed. Its use can be diminished about 70 per cent if the indications are reduced to: (1) malpresentation and (2) lack of satisfactory progress in labor. For maximum information pelvimetry should be carried out only while the patient is in labor.—*Arthur E. Childe, M.D.*

BRUSER, MICHAEL. A simple and accurate method of x-ray pelvimetry. *Radiology*, Oct. 1958, *71*, 565–569. (Address: Mall Medical Group, Memorial Blvd. at St. Mary's, Winnipeg 1, Manitoba, Canada.)

The author describes a simplified method of roentgen pelvimetry based on an isometric 90° triangulation technique which requires but two films. A special seat has been devised which consists of adjoining horizontal and vertical cassette chambers with an attached adjustable back rest. A metal scale is incorporated in the seat directly over the horizontal cassette chamber. The patient is placed in the special seat and the back rest adjusted to produce a true inlet film. The inlet and lateral films are successively exposed using a fixed target-film distance of 40 inches for both films. The corrected pelvic measurements are then taken directly from the films using a transparent correction scale which is described and illustrated. For more specific details the original article is recommended.

The advantages claimed for this technique are: it requires the technician to make only one measurement; namely, the focal-film distance; any error can readily be noted; and it is rapid and easy for the patient, requiring a minimum of movement and only two exposures. The author states in summary that although the technique is probably of maximum accuracy and simplicity, further experimentation and testing are required if optimum results are to be achieved. Criticism of the technique is invited.—*Edward B. Best, M.D.*

ROBERTS, LEONARD M., SQUIRE, JACK J., GUTTMACHER, ALAN F., and MARSHAK, RICHARD. Intrapartum lateral x-ray in the conduct of dystocic labors. *Am. J. Obst. & Gynec.*, Dec., 1958, *76*, 1306–1313. (From: The Departments of Obstetrics and Gynecology and Radiology, The Mount Sinai Hospital, New York, N. Y.)

This study was undertaken to assay the value of intrapartum roentgen-ray pelvimetry in the management of dystocia. The etiologic factors which make for dystocia are familar. In an effort to differentiate them and to plan therapy accordingly, the authors have come to rely in part on the lateral roentgenogram during labor, often repeated 2 or 3 times at intervals. With such help during dystocic labor, more accurate weight can be assigned to factors such as bony disproportion, malpresentation, inertia, and soft-tissue dystocia.

Fifty cases of dystocia in which a lateral roentgenogram was taken during labor have been submitted to analysis. One lateral roentgenogram was taken during labor in 39 cases, two lateral roentgenograms in 7, and three in 4. When more than one roentgenogram was necessary during labor, they were taken several hours apart. The large majority of the 50 patients has had roentgen-ray pelvimetry during the antepartum period because it was suspected clinically that some degree of pelvic contraction was present.

The interischial diameter is regarded as the transverse diameter of the midpelvis. The interspinous diameter, though traditionally reported, is regarded as unimportant because it is almost always posterior to the center of the pelvic cavity, the larger diameters of the head descending anterior to the spines. Furthermore, the length of the spines strongly affects the interspinous diameter and yet, long spines do not grealy influence the course of labor since their very length takes them further posterior to the center of the pelvic cavity.

Intrapartum pelvimetry has practically eliminated the trial of forceps on the obstetric service of

the Mount Sinai Hospital. This is a step in a conservative direction. With the aid of pitocin in bringing the head down and the use of roentgenograms to show the accurate level of the biparietal diameter, the ease or difficulty of instrumental delivery can be more accurately gauged.

The shortening of labor is of great importance and, as is well recognized, influences the perinatal mortality. Also, where there is borderline disproportion, sedation is frequently withheld in order not to diminish the force of contractions, but the use of analgesic medication in adequate amounts is often feasible and even desirable when intravenous pitocin stimulation is employed.—*Eugene J. McDonald, M.D.*

Kamieth, H. Geburtstraumen des Beckenringes vom Standpunkt der Röntgenologie. (Roentgenologic aspects of birth trauma to the pelvis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Dec., 1958, *89*, 694–701. (Address: Bahnhofstr. 31, Neunkirchen/Saar, Germany.)

The osteosclerotic changes in the region of the sacroiliac joints and the pubic symphysis, with particular reference to birth trauma, are discussed.

A true osteitis condensans ilii is seen in women only. Its diagnosis should be limited to bilateral sharply circumscribed juxtaarticular lesions, which show a triangular band-like sclerosis of the spongiosa, reaching at least the superior border of the ilium. It is always associated with pelvic relaxation. (The pelvic relaxation referred to herein is a pathologic form in contradistinction to the physiologic pelvic relaxation as seen in pregnancy.) In this series of osteitis condensans ilii, 17 out of 19 cases were in parous women, the remaining two were primigravidae close to term. Pathogenetically this seems to suggest that this osteosclerosis is an osteoblastic reaction due to excessive tension of the loosened ligaments, rather than a healing stage following their rupture in parturition.

Apart from this entity, the author recognizes small round, oval or triangular, sharply demarcated sclerotic foci in the region of the pubic symphysis and the sacroiliac joints, which do not have a common etiologic factor. These may represent a healing stage of traumatic rupture of ligaments and joint capsules, be it birth trauma or other, and are therefore naturally not limited to women only.

In relation to parturition, diastasis of the pubic symphysis can be regarded as a result of birth trauma. Not so pelvic relaxation however, which is an involutional failure secondary to excessive tension on the pelvic ligaments during pregnancy.—*Walter G. Heiman, M.D.*

Smith, Robert B. W., Sheehy, Thomas W., and Rothberg, Harvey. Hodgkin's disease and pregnancy; case reports and a discussion of the treatment of Hodgkin's disease and leukemia during pregnancy. *A.M.A. Arch. Int. Med.*, Nov., 1958, *102*, 777–789. (From: Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C.)

A total of 21 pregnancies in 18 patients occurred among 56 women with Hodgkin's disease at Walter Reed Army Hospital between 1942 and 1957. This prompted the authors to review their experience and the world literature on the effect of the disease and its treatment on pregnancy.

In general, Hodgkin's disease does not seem to affect pregnancy and pregnancy does not seem to affect the disease. Radiation therapy of sites distant from the uterus does not seem to affect the pregnancy nor the infant. No cases in which deliberate radiation of the pregnant uterus was given could be found.

Only 5 cases of pregnant women with Hodgkin's disease treated with alkylating drugs were reported in the literature but 17 more were found who were so treated for leukemia during pregnancy. Twelve normal infants resulted. However, experimental evidence in mice is cited as indicating that these drugs have teratogenic and abortifacient properties if given in the first trimester of pregnancy.—*Henry J. Klos, M.D.*

Paoletti, I., and Golfieri, G. L'impiego dei mezzi di contrasto tri-jodati nello studio radiologico del comportamento delle vie di escrezione urinaria durante lo stato gravidico-puerperale. (Use of tri-iodo contrast media in the study of excretory urography during pregnancy and puerperium.) *Ann. radiol. diag.*, 1958, *31*, No. 3, 203–224. (From: Istituto Ospedaliero Provinciale di Maternità, Bologna, Italy.)

The authors review a considerable amount of literature pertaining to changes of the urinary tract during pregnancy and puerperium and the theories which have been advanced to explain these changes by previous investigators.

Intravenous urography was done on 75 women, 61 were pregnant and 14 post partum. As far as the authors were able to determine, no deleterious effects either on the mother or fetus could be detected as a result of this procedure. The urinary tracts of the fetus were not visualized in any of their cases.

From these studies, the authors conclude that pyelo-ureteral alterations, (dilatations and displacements) occur in the early stages of pregnancy and increase in degree and frequency as the pregnancy progresses towards term. With the termination of pregnancy, they regress rapidly but may still be evident as long as one month later. It is their be-

lief, that the theories of functional and mechanical factors overlap in explaining the cause of these changes.

The authors were well satisfied with renografin, since it was well tolerated by the patient, and in a large majority of cases the urinary tract was well visualized. Excretion of the contrast medium in the pregnant patient is delayed and allowance in time for film exposure must be made.

The children, born after these studies were performed, were carefully studied and followed for various periods of time and nothing unusual was observed.—*Peter E. Russo, M.D.*

LISKER, M. Modificaciones urologicas en el embarazo. (Urologic complications in pregnancy.) *Rev. urol., México*, Sept.–Oct., 1958, *16*, 225–233.

In most patients there is unilateral or bilateral dilatation of the ureter or of the ureter and renal pelvis during gestation. When the dilatation is unilateral, it is more likely to be on the right side.

Experiments undertaken in nonpregnant patients indicate that hormones decrease the tone of the ureter.

Usually the pregnancy goes to full term in spite of serious anomalies of position of the kidneys. The fetal mortality is elevated in these patients with renal ectopia.—*Charles M. Nice, Jr., M.D.*

LOWMAN, R. M., DONNELLAN, E., and GOLDENTHAL, S. Radiation reduction in diagnostic obstetrical radiography: The application of electronic photographic techniques. *Am. J. Obst. & Gynec.*, Jan., 1959, *77*, 18–27. (From: The Department of Radiology, The Memorial Unit, Grace-New Haven Community Hospital, Yale Medical Center, New Haven, Conn.)

The authors stress the necessity for reducing the exposure dose in diagnostic obstetrical roentgenology. Such studies should be restricted to those cases in which critical information regarding major obstetrical problems may be obtained. Techniques which require increased dose exposure should be discarded.

Reduction of radiation exposure is commonly accomplished by increased aluminum filtration of the primary beam, high speed screen combinations, high kilovoltage technique, higher speed films and improved processing chemicals.

The authors have also investigated the electronic printing device as an additional method of reducing radiation exposure. Using deliberate underexposure with subsequent revision by automatic compensating electronic devices, they found it possible to reduce radiation in anteroposterior roentgenograms by a further 60 per cent and in lateral roentgenograms by a further 40 per cent. Such a device can also be used to avoid re-examination of the maternal pelvis when unsatisfactory exposures have been completed.—*Arthur E. Childe, M.D.*

REISS, H. E., and GROSSMANN, MARIA E. Experience with new contrast media for hysterosalpingography. *J. Obst. & Gynaec. Brit. Emp.*, Oct., 1958, *65*, 782–787. (From: The Obstetric Unit and X-ray Diagnostic Department, University College Hospital, London, England.)

Since the first injection of a radiopaque substance into the uterine cavity in 1910, the search for an ideal contrast medium has continued. Rubin (1941) has restated the properties of an ideal contrast medium for hysterosalpingography: that it should be adequately opaque, rapidly absorbed, nonirritant, moderately viscous, and capable of being sterilized.

Water-soluble contrast media, with their rapid and complete absorption, avoid the chief risks enumerated; intravasation, if it occurs, is free from danger. The low viscosity permits accurate delineation of the uterine and tubal cavities, reveals minute details of their mucosal pattern, and ensures quick spill which enables rapid diagnoses to be made, with saving in time and irradiation. Furthermore, the media mingle readily and completely with the contents of a hydrosalpinx.

However, the unduly low viscosity of water-soluble contrast media may have one great disadvantage: as Rubin and Morse (1939) pointed out, the crystalline iodine compounds used in excretory urography pass through the tubes so quickly that the latter are hardly outlined and are rapidly overshadowed by the spill into the peritoneal cavity. For this reason various thickening agents have been added.

The authors have re-examined the 200 hysterosalpingograms in this series and believe that in urografin 76 per cent, used in the last 148 of these cases, they have found the most satisfactory contrast medium at present available. It is safe, mixes well with body secretions and the contents of hydrosalpinges, and gives satisfactory contrast without obscuring fine details. It is completely absorbed in a short time, and in the majority of cases 2 roentgenograms are adequate for diagnostic purposes. Intravasation is devoid of risk, and screening is not necessary to guard against this complication.

The authors have contrasted their water-soluble agents only against lipiodol which has long since been superseded by greatly improved and less viscous agents such as ethiodol. This agent and other similar less rapidly absorbed contrast media are not mentioned.—*Eugene J. McDonald, M.D.*

GENITOURINARY SYSTEM

OCHSNER, SEYMOUR, and BURNS, EDGAR. Ureteritis cystica and pyelitis cystica. *South.*

M. J., Aug., 1958, *51*, 951–955. (From: The Departments of Radiology and Urology, Ochsner Clinic, and Tulane University School of Medicine, New Orleans, La.)

Cystic changes in the mucosal lining of the urinary tract are commonly visualized by urologists during cystoscopic study and may be demonstrated roentgenologically in the upper urinary tract by excretory urography. The cysts are usually seen in the region of the trigone and ureteral orifices. Grossly, they appear as discrete translucent or gray, cyst-like bodies, 1 to 2 mm. in diameter, scattered on the mucosal surface. Some are superficial and others are deeper in the mucosa. The lesions are considered by most observers to be sequelae of chronic or recurrent infection of the urinary tract.

Clinical and urographic data are presented on 8 cases of pyelo-ureteritis cystica. The roentgenographic appearance is usually one of clusters of small round smooth filling defects. They must be differentiated from air bubbles, stones, papillary tumors, blood clots, and tuberculous pyelo-ureteritis.—*John F. Weigen, M.D.*

Scholtze, H., and Albrecht, K. F. Röntgenologische Studien an den ableitenden Harnwegen nach Lungenangiographie mit grossen Kontrastmittelmengen bei Lungentuberkulose. (Roentgenologic studies of the urinary tract following pulmonary angiography with large doses of contrast media in tuberculosis of the lung.) *Tuberkulosearzt*, Nov., 1958, *12*, 717–721. (Address: H. Scholtze, Sanatorium Sonnenblick, Marburg/Lahn, Germany.)

Angiography of the pulmonary vessels was performed in 200 patients with tuberculosis of the lung. This was a preoperative procedure for segmental resection or lobectomy. The contrast medium used was urografin (identical with renografin). In 50 patients, who received between 100 and 250 ml. urografin per examination, renal excretion studies were also done. Minor sensitivity phenomena were observed in some of these cases.

The renal shadow was clearly visualized by nephrography in all cases, but the collecting structures were demonstrated in only two-thirds of the 50 patients. A probably specific lesion of the kidney was observed in 6 cases and congenital anomalies of no pathologic significance in 8 patients. There was a marked dilatation of the ureter in 90 per cent of the patients. The causes of this are discussed. The gallbladder or the extrahepatic bile ducts were never visualized.—*Eckart Schackow, M.D.*

Skeletal System

Lefebvre, J., and Chaumont, P. Le devenir du granulome éosinophile chez l'enfant. (Evolution of eosinophilic granuloma in infants.) *J. de radiol., d'électrol. et de méd. nucléaire*, Nov., 1958, *39*, 705–712. (From: Service central d'Electroradiologie de l'Hôpital des Enfants malades, Paris, France.)

Eosinophilic granuloma has been presented in most of the recent French publications as a benign condition resulting in cure in contrast to the other reticuloses. The present study is based on 13 cases with ages ranging from eighteen months to fourteen years in which the disease was manifested at first by localized osseous lesions, confirmed histologically.

According to the authors, the roentgen aspect of eosinophilic granuloma is of little prognostic significance, since 2 of the 13 cases in which the roentgenographic examination suggested a possible malignant change have run a benign course and were cured. In the remaining 11 cases, there was a punched out radiolucent area, oval or polycyclic, without marginal sclerosis, typical of benign eosinophilic granuloma.

Four of the patients were under two years of age and later showed visceral infiltration, particularly pulmonary, and died. Statistically the young age, because of potential visceral involvement, proved to be the most valuable prognostic factor.

The multiplicity of osseous lesions is not so important for prognosis as long as there is no visceral infiltration. Extensive skull lesions would bring about a bad prognosis only because of a possible complicating diabetes insipidus. Vertebral involvement in the cervical area is considered by the authors to be serious because of its proximity to the medulla oblongata in case of a subluxation. In two of the cases, lesions localized to the dorsal spine were healed and led to the formation of vertebra plana.

In conclusion, the evolution of eosinophilic granuloma is capricious and unpredictable. Statistically, age appears to be the factor of greatest importance. A roentgenologic picture typical of eosinophilic granuloma does not preclude evolution toward a more serious form, probably terminating in death, if a complicating visceral and particularly pulmonary involvement supervenes.—*Henri-Paul Lévesque, M.D.*

Foster, John H., and Kirtley, James A. Unilateral lower extremity hypertrophy. *Surg., Gynec. & Obst.*, Jan., 1959, *108*, 35–42. (From: The Department of Surgery, Vanderbilt University School of Medicine, and the Surgical Service, Vanderbilt University Hospital, Nashville, Tenn.)

The Klippel-Trenaunay syndrome consisting of (1) osseous and soft tissue hypertrophy of the lower extremity; (2) varicose veins of the extremity present from infancy; and (3) a hemangioma of the skin of the extremity has been the subject of reports since 1900. While hemangiomata were inconstantly

seen in the cases reported, some form of venous obstruction was usually present.

The authors describe 4 cases of unilateral hypertrophy of the lower extremity. Varicose veins were present in each case; hemangiomata in 3. Proof of venous obstruction was obtained by roentgenographic or surgical means in 2 of the cases. In a third case, venography was attempted on three occasions and although no obstruction was seen complete filling was never obtained. Scanograms, when obtained, showed that true osseous hypertrophy was present in the involved extremity. Circumferential enlargement was present in all, but whether it was due to edema or to true soft tissue hypertrophy could not be ascertained.

Atresia of the common, internal and external iliac veins was noted in one patient. Without benefit of prior venography, a saphenous ligation and stripping operation were performed with resultant increase in varicosity and the production of hypertrophy which was not previously present. Venography was then performed and the atresia demonstrated. A subsequent grafting procedure resulted in arrest of the process. The importance of angiography in proper evaluation of the patient with unilateral limb hypertrophy is stressed.

The case material and earlier investigations would indicate that unilateral lower extremity hypertrophy is due to hyperemia, most commonly because of venous stasis or venous hypertension, the hyperemia acting as a stimulus to the epiphysis.—*Jack Reynolds, M.D.*

FISHER, SAMUEL H. Skeletal manifestations of parent-induced trauma in infants and children. *South. M. J.*, Aug., 1958, *51*, 956–960, (From: The Department of Radiology Greenville General Hospital, Greenville S. C.)

Chronic injury due to adult trauma produces roentgen changes which have become an established entity. The cause of the patient's injuries may be unrecognized until suggested by the roentgen findings.

Trauma to children may be categorized as: unavoidable episodes in stable households, a family environment which momentarily or periodically may not afford the usual protective atmosphere, and the presence of aggressive, immature, or emotionally ill adults.

Six cases of parent-induced trauma in infants and children are presented. Two cases resulted in death of the child. One of the cases showed extreme roentgen changes and this is illustrated.

By recognizing the entity of trauma by adults, not only may much time and effort be saved in arriving at a diagnosis but, more important, if law enforcement agencies are able to act, life may be saved.—*John F. Weigen, M.D.*

SHERMAN, ROBERT S., and GLAUSER, OSCAR J. Radiological identification of fibrous dysplasia of the jaws. *Radiology*, Oct., 1958, *71*, 553–558. (Address: R. S. Sherman, 444 East 68th St., New York 21, N. Y.)

Seventeen histologically proved cases of fibrous dysplasia of the jaws were studied roentgenologically, to form a basis for the roentgen interpretation of that disease. Fifteen of the 17 cases were monostotic. One patient had involvement of the maxilla and the zygoma and in the other the mandible and both maxillae were involved. Eleven patients were female and six were male. The age range was eight to forty-four years, with over half of the patients between eight and fourteen years. The usual complaints were painless swelling with asymmetry of the face and disturbance in position of the teeth. Excision or curettage was performed 14 times, but in 3 instances the lesion was only biopsied. Except for one patient with a recurrence after one year, all were apparently clinically free of disease or unchanged after a follow-up of several years.

Three fairly distinct roentgenographic types occur. The first and probably the most diagnostic of these shows a diffuse, uniform, homogeneous sclerosis. The sclerotic form tends to follow the general contours of the bone producing enlargement. This type was found only in the maxilla in this series. This variety bears a superficial resemblance to osteitis deformans, sclerosing cancer metastases, and possibly the sclerosing type of osteogenic sarcoma. The multiloculated, cystic type is most frequently seen in the maxilla. It is somewhat less specific in its roentgen appearance but is still considered to be highly suggestive of fibrous dysplasia. This variety is quite lytic in character, oval in shape, with septa or ridges, a fairly sharp border, cortical thinning and expansion and frequently calcific strands or flecks. The least specific roentgen type of fibrous dysplasia is the unilocular pattern. A clear distinction between this type and ossifying fibroma is not always possible.—*Arno W. Sommer, M.D.*

IWATA, SENNAN, and COLEY, BRADLEY L. Report of six cases of chondromyxoid fibroma of bone. *Surg., Gynec. & Obst.*, Nov., 1958, *107*, 571–576. (From: The Bone Tumor Service, Memorial Cancer Center, New York, N. Y.)

In 1948 Jaffe and Lichtenstein first described a rare bone lesion called chondromyxoid fibroma. It is a benign tumor derived from cartilage forming connective tissue. There have been 30 cases previously reported and the authors add 6 more. The lesion is seen mostly in adolescents. Males and females are affected with equal frequency. The bones of the lower extremity are involved most commonly. In the authors' group the lesion was present in the femur or tibia in fully one-half of the cases. The lesions

involve the metaphysis and often extend to involve the adjacent diaphysis. Pain and swelling are the common symptoms and they develop slowly and insidiously.

The roentgen appearance mimics chondroma, benign chondroblastoma, bone cyst and even fibrous dysplasia. Some have been mistakenly called giant cell tumors. Resection of the tumor in the fibula, rib, ulna or metatarsal bones or curettage in weight bearing bones is the treatment advocated. The lesions are not sensitive to roentgen therapy.

In one of the cases there was a secondary chondrosarcomatous degeneration in the chondromyxoid fibroma. Such malignant transformation has not been reported previously. It is desirable to consider this benign tumor in all lytic bone lesions in order to avoid unnecessary amputations.—*Frank M. Windrow, M.D.*

Thieffry, Stéphane, and Sorrel-Dejerine, Jacqueline. (Paris, France.) Forme spéciale d'ostéolyse essentielle héréditaire et familiale à stabilisation spontanée, survenant dans l'enfance. (A special form of idiopathic hereditary and familial osteolysis with spontaneous stabilization occurring in childhood.) *Presse méd.*, Nov. 26, 1958, *66*, 1858–1861.

The authors report 5 cases of a hereditary and familiar affection among 3 generations which begins in early childhood and is characterized by spontaneous osteolysis of carpal and tarsal bones in which ossification apparently had been proceeding normally. The osteolysis stabilizes spontaneously in late childhood, without affecting other parts of the skeleton except inconstantly those bones which are in contact with the carpals and tarsals. Morphologic craniofacial anomalies accompany this osteolysis, which is probably a dominant mendelian trait.—*Frank A. Riebel, M.D.*

Rosen, Irwin E. Unusual intrameniscal lunulae; three case reports. *J. Bone & Joint Surg.*, July, 1958, *40-A*, 925–928. (From: The Surgical Service, United States Air Force Hospital, Keesler Air Force Base, Miss.)

The author gives 3 case reports of the rare presence of a sesamoid structure within the medial meniscus of the knee. Pearson described these ossicles in the meniscus and called them lunulae.

Their clinical importance lies in the fact that they should not be interpreted as loose bodies in order to avoid fruitless exploration of the knee.

A review of the literature showed varied opinions as to whether they are secondary to trauma with heterotopic bone formation or whether they represent vestigial structures. Harris explained that the ossicles were the result of mucoid degeneration. Weaver pointed to the existence of primary and the more common secondary types which occurred after trauma. Pederson found ossicles frequently present in menisci of rodents without evidence of disease and concluded that in man they were a vestigial structure.

In the author's cases the lunulae were in the posterior horn of the medial meniscus. All three cases were operated upon, pathologically proved, and had uneventful recovery.

The author feels that these ossicles are vestigial structures, and that they give rise to mild symptoms of derangement of the knee because of protruding contours which interfere with normal joint function. —*Roscoe E. Miller, M.D.*

Verbrugge, J., and Verjans, H. Lesions rares des cartilages de croissance du genou. (Rare lesions of the growth cartilages of the knee.) *Acta chir. belg.*, April, 1958, *57*, 299–318. (Address: Chaire de Chirurgie orthopédique de l'Université de Gand, Gand, Belgium.)

The authors present 5 cases in which apparently minimal and unusual causes affecting the growth cartilages of the knee have had great consequences, bringing about marked disability and deformity. The authors have purposely excluded the usual causes of shortening or lengthening, with consequent diaphyseal fractures, resulting from poliomyelitis and infectious diseases.

Case I. A female, normal delivery at birth, had a small port wine type hemangioma at the outer aspect of the right knee. Deep roentgen therapy with unknown dosage was administered. During subsequent years marked deformity and shortening resulted, with epiphysiodesis involving the outer third of the distal femoral epiphysis. Several surgical procedures were required for correction.

Case II. An eleven year old healthy male, a victim of an exploding shell during a 1942 bombardment, sustained a penetrating splinter (3×1.5 cm.) injury at the medial aspect of the knee involving the inner third of the epiphyseal cartilage. The foreign body was removed and immediate healing occurred. When next seen in 1944, the patient had a pronounced genu varum deformity and epiphysiodesis of the medial third of the cartilage had developed. Corrective surgical intervention was performed. However, the patient died in a subsequent bombing in 1945.

Case III. A seventeen year old healthy female was involved in an automobile accident in 1952 with several injuries to the body, including the inner aspect of the knee and distal femur, all of which healed following adequate care. Two years later, a marked genu varum deformity was noted. A soft tissue scar was present at the site of injury and closure of the inner one-third of the epiphysis was demonstrated roentgenologically.

Case IV. A twelve year old healthy female, normal at birth, had two superficial hemangiomas, one on

the scalp and one at the external aspect of the left knee. The latter received deep roentgen therapy shortly after birth. The dosage and manner of treatment are unknown to the authors. The hemangioma disappeared, but an open sore (third degree reaction) occurred at the site of the treatment. When seen, marked genu varum deformity was present with considerable shortening and epiphysiodesis of the outer aspect of the distal femoral epiphysis.

Case v. A fifteen year old male, normal delivery, walked at one year, with excessive weight for the patient's age developed progressive deformity, which became more pronounced with growth, resulting in a concavity at the inner aspect of the right knee (varus deformity). A provisional diagnosis of osteochondrosis deformans was made. Repeated corrective surgical procedures were performed as seemed indicated.

The authors warn against the use of radiation therapy for the treatment of hemangiomas in cases such as those listed above.

Seventeen figures with reproductions of roentgenograms, sketches and diagrams accompany this article.—*William H. Shehadi, M.D.*

Melamed, Abraham. Some anatomical and roentgenologic considerations with respect to the lumbosacral spine; with special reference to retrodisplacement. *Radiology*, Oct., 1958, *71*, 548–552. (Address: Evangelical Deaconess Hospital, 620 N. 19th St., Milwaukee 3, Wisc.)

The study reported here was undertaken to determine the pathogenesis of retrodisplacement of lumbar vertebrae. Thirty-four articulated human spine specimens were studied. The commonly accepted theory is that retrodisplacement is due to the downward and posterior inclination of the articular facets, implying that when intervertebral disk narrowing occurs, the cephalad vertebra is forced downward and backward. The author found, however, that in almost all specimens, by direct measurement, the vertical axis of the facets formed a 90° angle, or very close to a 90° angle with the horizontal surface of the vertebral body. In other words, there was little or no posterior angulation of the facets. It was also found that by narrowing the intervertebral space and/or by subluxating the articular facets retrodisplacement did not occur. For these reasons the author contends that other factors must enter into the causation of retrodisplacement. In the intact spine the center of gravity of the body passes through the third lumbar vertebral body. If for any reason this is shifted backward, one prerequisite for the development of retrodisplacement is fulfilled. Eventually the integrity of the intervertebral disks, apophyseal joint capsules and spinal ligaments is disturbed by the shearing force of gravity and malalignment develops. The greater frequency of retrodisplacement in the upper lumbar region occurs because changes in the center of gravity occur and are reflected here earliest.

Retrodisplacement is easily diagnosed in the lateral projection in most cases. However, interpretation of the lateral roentgenogram must be made with caution especially at the lumbosacral level. The anteroposterior diameter of the fifth lumbar vertebra is greater than that of the sacrum in 70 to 80 per cent of all patients. This gives rise to an apparent overlap of the posterior margins which may occasionally be interpreted as retrodisplacement.

As an aid to correct evaluation of the lateral projection of the lumbosacral spine, the author follows the curve formed by the anterior borders of the spinal canal. In the average case this line will pass through the posterior inferior flaring of the fifth lumbar vertebra. If this line is in any way distorted, true displacement should be suspected and confirmed by other criteria.—*Z. Petrany, M.D.*

Blood and Lymph System

Dotter, Charles T., and Frische, Louis H. Visualization of the coronary circulation by occlusion aortography: A practical method. *Radiology*, Oct., 1958, *71*, 502–524. (Address: C. T. Dotter, University of Oregon Medical School, 3181 S. W. Sam Jackson Park Road, Portland 1, Ore.)

This report describes a technique for coronary angiography which has been found to be safe and reliable in the dog. The authors believe it is ready for application to the study of the diseased coronary arteries of man.

In the procedure which the authors used, a special double lumen balloon catheter was used to inject a contrast substance into the proximal aorta during a period of brief but total occlusion of the ascending aorta just above the site of injection. All the contrast substance enters the coronary arteries, thereby allowing clear visualization. Other investigators have reported *in vivo* contrast studies of the coronary arteries, but the authors claim important advantages for their method.

A light general anesthetic is preferred for the procedure. Under fluoroscopic control the catheter is introduced into the radial artery and advanced until the tip reaches a position about an inch above the estimated site of the aortic valves. Trial inflation of the balloon is carried out by injection of nitrous oxide or carbon dioxide. Complete occlusion must be obtained if the examination is to be successful. Occlusion should not exceed five or ten seconds. Once the correct position of the catheter and volume of gas necessary for complete occlusion have been determined, the examination is carried out. As soon as complete occlusion of the aorta is obtained, the injection of contrast substance is injected in three

seconds or less. Simultaneously with the beginning of the injection, a series of roentgen-ray exposures is started and continued for six or eight seconds. Deflation of the balloon is allowed to take place at the end of the injection. Continuous electrocardiographic monitoring should be conducted during and following all occlusions.

Experimental observations were made on a series of 51 dogs in order to determine the feasibility of this procedure. Over 500 complete occlusions of the ascending aorta were produced without death or evidence of serious consequence. Various opaque media were subjected to trial, including hypaque, urokon, miokon and thorotrast. The most satisfactory medium was found to be thorotrast. In spite of its alpha activity and its alleged carcinogenic properties, thorotrast probably is the safest medium for this procedure.

The use of occlusion catheters in the cardiovascular system promises to open up many unexplored clinical and experimental areas of importance, examples of which are (a) new techniques for cardiovascular visualization, (b) elective controlled cardiac arrest in the intact subject for purposes such as cardiovascular visualization and (c) total cardiopulmonary bypass as an emergency therapeutic measure in the intact patient.—*Arno W. Sommer, M.D.*

Thal, Alan P., Richards, L. Stephen, Greenspan, Richard, and Murray, M. John. Arteriographic studies of the coronary arteries in ischemic heart disease. *J.A.M.A.*, Dec. 20, 1958, *168*, 2104–2109. (From: The Departments of Surgery, Radiology, and Medicine, University of Minnesota Medical School, Minneapolis, Minn.)

Visualization of the coronary vessels can be obtained in unanesthetized patients without risk. The technique is described in detail. It is important to have roentgenograms in both anteroposterior and lateral views. These are obtained by using a biplane rapid film changer. The Schönander unit allows 6 films per second in two planes.

Complete or partial occlusion of a major vessel is a most definite sign. Other signs are tapering of the vessel, atheromatous encroachment on the lumen and complete or abrupt obstruction to contrast medium. The collateral circulation can often be visualized.

The surprising finding was that in several cases, with typical angina at rest and on exertion, normal coronary arteriograms were found, and the patient's symptoms promptly disappeared. This makes the study very valuable in determining which candidates might benefit from surgery.

In addition to the diagnostic value of the coronary arteriograms, it is possible to formulate from them a more accurate prognosis in coronary sclerosis based on such factors as the extent of the disease and collateral circulation.

Review of 4 cases and excellent reproductions of arteriograms with diagrams showing coronary vessels and collateral circulation are included in this paper. —*Eva S. Carey, M.D.*

Bonte, G., Caron, J., Pauchant, M., and Gérard, A. Examen de l'aorte thoracique et du ventricule gauche par cathétérisme intraventriculaire à partir de la fémorale. (Study of the thoracic aorta and left ventricle by means of intraventricular catheterization via the femoral artery. *J. de radiol., d'électrol. et de méd. nucléaire*, Oct., 1958, *39*, 593–598. (From: Service d'Electroradiologie (Ouest), Hôpital régional, Cité hospitalière, Lille, France.)

Intravenous or selective angiocardiography gives only limited information on left heart pathology. Direct puncture of the left auricle or ventricle allows the recording of pressure curves, but opacification of the left chambers is rarely performed through these means because it necessitates the use of a large traumatizing trocar. The authors recommend retrograde catheterization of the left ventricle via the femoral artery with the aid of Seldinger's method. Until now, they have performed 14 ventriculographies with success in patients suffering either from congenital or acquired cardiopathies or from a mediastinal disease justifying thoracic opacification.

The indications of such a procedure should be discussed by the whole team and the catheterization should be performed only when there is hope of a possible surgical treatment.—*Maurice Dufresne, M.D.*

Bulgrin, James G., and Jacobson, George. Aortographic demonstration of an aortocaval fistula; a case report. *Radiology*, Sept., 1958, *71*, 409–411. (Address: 1200 N. State St., Los Angeles 33, Calif.)

A case of nontraumatic aortocaval fistula complicating arteriosclerotic aneurysm of the abdominal aorta is reported. Of the 5 other cases which have been reported since 1909, 1 was associated with an underlying syphilitic abdominal aortic aneurysm and the other 4 followed bullet wounds. In only one instance was there even mention of arteriographic study. Duration of the fistula varied from four months to twelve years. The degree of cardiovascular disturbance appeared to be related directly to the duration of the lesion.

The case reported concerns a sixty-eight year old white male, with a history of controlled diabetes for eight months and mild congestive failure for two months, who was hospitalized because of a sudden attack of severe, generalized, nonradiating chest pain

which occurred initially while straining at stool and recurred one day later. On admission and during his hospital course the patient showed signs of congestive failure but his blood pressure was normal and repeated electrocardiograms showed no evidence of coronary occlusion. The most significant physical finding was a loud bruit over the entire abdomen and back. There was no evidence of syphilis. Roentgenograms of the chest demonstrated cardiac enlargement, pulmonary congestion, and moderate bilateral hydrothorax. Roentgenograms of the abdomen showed a calcified abdominal aortic aneurysm. Translumbar percutaneous aortography was performed in a normal manner. The aneurysm and the aorta distal to the puncture site were very faintly opacified and the opaque material, almost in its entirety, entered the dilated vena cava. Subsequent operation disclosed an arteriosclerotic abdominal aortic aneurysm below the renal vessels, complicated by a communication between the aorta and vena cava, 1 cm. in diameter. In the course of reparative surgery the patient succumbed to cardiac arrest. Autopsy was not performed.—*Walter H. Jarvis, Jr., M.D.*

Leger, Lucien, and Roy-Camille, Raymond. Anastomose porto-cave; Étude pré- et post-opératoire de 12 observations. (Porto-caval anastomosis: Pre- and postoperative study of 12 cases.) *Presse méd.*, Oct. 29, 1958, *66*, 1673–1676. (From: Hôpital Lariboisière, Paris, France.)

These cases were studied by splenic manometry which truly reflects portal pressure and splenoportography for stasis, reflux, preoperative collateralization and postoperative shunt permeability.

Portal pressure progressively decreases after the establishment of a shunt but not always immediately. Only one case was an exception which also was unusual in that the patient died of hemorrhage after one year. Coronary or mesenteric reflux giving rise to stasis disappears. Esophageal varices are smaller but the change may be slow in appearing. Serial splenoportograms demonstrate functioning of the shunt with massive penetration of the contrast substance into the inferior vena cava. The studies of liver tests are not yet complete enough to justify conclusions.—*Marcy L. Sussman, M.D.*

Fesani, F., and Uleri, G. Possibilità e limiti dell'indagine arteriografica nell'infanzia. (Feasibility and limitations of arteriography in infants.) *Ann. ital. di chir.*, 1958, *35*, No. 3, 179–208. (From: Istituto di Clinica Chirurgica Generale e Terapia Chirurgica, and Istituto di Radiologia e del Radium dell'Università, Parma, Italy.)

The authors stress the importance of arteriographic examinations in the adult. They consider the possibility of extending the method more generally in the infant and discuss principally the limitations defined by previous investigators. They throw additional light on the subject by presenting a number of interesting cases.

The limits, which must be recognized, include the problems of: (1) anesthesia; (2) chemical toxicology; (3) technical roentgenography; and (4) anatomy.

The criteria to be followed in anesthetizing an infant who is to undergo arteriography have been previously established. Venipuncture and injection of the contrast material have been known to produce vasospasm. The use of intravenous barbiturates is accompanied by vasodilatation. It is desirable that the infant be under deep narcosis so that proper roentgenographic images may be obtained and to minimize the danger of circulatory and respiratory reactions. The authors describe a method of general anesthesia which has proved to be satisfactory in their hands.

The intolerance to the contrast medium must be determined and, if present, constitutes an absolute contraindication. A possible complication is the direct injection of the opaque medium in the renal artery, particularly if under high pressure, so that renal damage is caused. Because of the relatively small lumen of the vascular channels in infants, great caution must be employed to avoid injury to the vessels and extravasation. The consequences are difficulty in roentgenographic interpretation and morbidity.

Catheterization may avoid many undesirable sequelae of venous or arterial puncture. Besides it permits under fluoroscopic control localization of the catheter and of the desired level for injection of the contrast material.

Adequate angiographic technical equipment is of paramount importance.

The authors report cases with the following lesions: stenosis of the pulmonary artery, tetralogy of Fallot, retroperitoneal ganglioneuroma, and hydronephrosis secondary to an aberrant vessel.—*Anthony A. Blasi, M.D.*

Gollman, G. Der Beitrag der Angiographie zur Differenzierung blastomatöser und entzündlicher ossärer und parossärer Erkrankungen. (Angiography in the differentiation between neoplastic and inflammatory processes of the osseous and paraosseal tissues.) *Radiologia Austriaca*, 1958, *10*, No. 1, 49–54. (From: Zentralröntgen- und Radiuminstitut des Landeskrankenhauses, Graz, Austria.)

Arteriography may be a very helpful procedure in certain cases for differentiating between neoplastic and infectious diseases.

The angiographic features in favor of a tumor are: (1) formation of a blood circulation of its own, (2) displacement of arteries and veins, and (3) presence

of a tumor-stain or localized relative absence of blood vessels.

Displacement of blood vessels is, however, difficult to demonstrate in areas with a small blood flow under normal conditions. Since the vascular system of the bones cannot be visualized with routine angiography, a bone tumor can be recognized on angiograms only in cases with periosteal involvement.

The angiographic criteria in favor of an inflammatory process are less obvious and comprise: (1) narrowing or dilatation of blood vessels and (2) abnormal phases of blood flow on serial roentgenograms.

The most helpful finding in the differential diagnosis between tumor and infectious process is the formation of a characteristic blood circulation in the tumor. Displacement of blood vessels, on the other hand, is not specific and can be caused by tumors as well as by abscesses.

The author feels that in certain cases a differentiation between benign and malignant tumors is facilitated by arteriography. Irregularly shaped, reticular, and lake-like blood vessels which show premature filling as seen in arteriovenous fistulas favor but are not conclusive for a malignant neoplasm. In addition, the vascular supply was found to be ill-defined in malignant tumors.

The included roentgenograms illustrate the value of arteriography in the differential diagnosis between Ewing's tumor, osteomyelitis and other lesions.—*Wolfgang H. Steinmetz, M.D.*

Short, D. S. Arteries of intestinal wall in systemic hypertension. *Lancet*, Dec. 13, 1958, *2*, 1261–1263. (From Middlesex Hospital Medical School, London, W. 1, England.)

In cases of systemic hypertension postmortem arteriography was employed to study the arterial bed of the small intestine. A bismuth oxychloride-gelatin suspension was injected into the superior mesenteric artery and, after fixation, strips of intestinal wall were roentgenographed. These roentgenograms were then compared with histologic sections. The number of vessels in a given area and the size of the lumen were determined from the roentgenograms.

In 4 of 6 cases of hypertension, the number and diameter of the arteries were decreased. Histologic sections indicated that the decrease in caliber was due to structural narrowing rather than functional spasm.—*Leslie K. Sycamore, M.D.*

General

Lefroy, R. B. The Nisbet Symposium: Collagen disease. Part I. General aspects. *Proc. Coll. Radiologists, Australasia*, Sept., 1958, *2*, 1–5.

The author discusses the basic formation of connective tissue and the factors concerned in its production and maintenance. He prefers the title of "connective tissue disorders" to "collagen diseases" because collagen is often not the main factor involved and because it is merely one part of connective tissue.

Connective tissue varies in its consistency from the fixed character of bone to the fluid nature of jelly in the umbilical cord. It is composed of fibers, mainly collagen, fibroblasts and "ground substance." Collagen is apparently produced by fibroblasts and ground substance. While collagen is a static end product of connective tissue, it is a dynamic tissue appearing in many different forms and is subject to change. The "ground substance" is a sort of plastic fluid containing water, electrolytes and colloids.

Connective tissue appears to be guided by three main influences: enzymes, hormones and vitamins. The enzymes concerned are the hyaluronidases and heparin. The adrenal and sex hormones besides thyroxin make up the important hormones. The vitamin of importance is ascorbic acid.

The "connective tissue disorders" are manifested by proliferation and degeneration. Rheumatoid arthritis, rheumatic fever and scleroderma represent the proliferative phase. On the other hand, rheumatic fever, rheumatoid arthritis, lupus erythematosus and dermatomyositis all show changes which are classified as mucoid degeneration.

Fibrinoid degeneration or necrosis has been linked most often with the collagen diseases. It was believed initially that fibrinoid originated from degenerate collagen. In disseminated lupus erythematosus, fibrinoid is apparently a degraded form of nucleic acid, one of the essential elements of cell protein. These changes are specific for disseminated lupus erythematosus, and the fibrinoid seen in other connective tissue disorders probably has a different origin. Collagen has been produced in the rabbit by the injection of a foreign protein. On the basis of hypersensitivity, attempts have been made to hold one etiologic factor responsible. Klinge's list of collagen diseases is quite lengthy and includes endocarditis and malignant nephrosclerosis as diseases of hypersensitive origin containing fibrinoid. Peptic ulceration and malignant hypertension should not be included in this group because of the presence of other factors.

The author believes that in order to gain a better appreciation of these disorders we should: (1) shift the spotlight away from the name "collagen," (2) resist the suggestion that fibrinoid has its origin from collagen in all cases, and (3) believe there is not necessarily, merely one etiologic factor responsible for these disorders. Rheumatic fever and polyarteritis nodosa are both closely connected with hypersensitivity. Disseminated lupus erythematosus is related to some extent to hypersensitivity. Rheumatoid arthritis shows no impressive clinical evidence for the role of hypersensitivity. Amyloidosis and myelomatosis are included in this group. Etiologic factors are

obscure, but it seems likely that further knowledge will come from a study of globulin fractions and immune responses rather than of the histologic characteristics of collagen.—*J. N. Ané, M.D.*

Goatcher, Phyllis B. E. The Nisbet Symposium: Collagen disease. Part II. The arthritides. *Proc. Coll. Radiologists, Australasia*, Sept., 1958, *2*, 5–10.

The author emphasizes the importance of early accurate diagnosis in the treatment of the arthritides. While it has been taught for many years that rheumatoid arthritis is a disease of young women, it has been shown in a large series of cases that the average age of onset is forty-one years.

Age and sex are of importance in the diagnosis of rheumatoid arthritis. The young man with peripheral joint disease should have a roentgenographic examination of his sacroiliac articulations to exclude ankylosing spondylitis and should be checked for urethral discharge. Urethral infection may be the cause of a rheumatoid type of arthritis which improves on treatment of the discharge. Ford has reported some cases developing a true ankylosing spondylitis after persistent urethritis.

Gout occurs in men in 95 per cent of the cases, and in women, usually after the menopause, in 5 per cent. Rheumatoid arthritis may have a sudden onset and many cases in this group are diagnosed erroneously as gout.

Since rheumatoid arthritis is regarded as a systemic disease with wide spread connective tissue involvement, laboratory tests are becoming increasingly useful. The blood sedimentation rate and the hemoglobin tests are the most widely used methods of investigation. These tests are probably of greatest value in the prodromal stage of rheumatoid arthritis and also in the early diagnosis of cases labelled tenosynovitis capsulitis of the shoulder or metatarsalgia. In a series of patients with persistently raised blood sedimentation rates, many subsequently developed rheumatoid arthritis.

The Rose test is based upon the observations made by Waaler and by Rose independently that the serum of patients with rheumatoid arthritis agglutinates the sensitized red blood cells of sheep. Positive results have ranged from 48 per cent to 89 per cent of the sera from rheumatoid patients. Rheumatic fever appears to be the only one of the major "connective tissue" diseases which gives consistently negative results. The Rose test does not reflect clinical changes associated with treatment of rheumatoid arthritis and remains negative in some patients despite severe progressive disease.

Since the serology in rheumatoid arthritis and lupus erythematosus is similar, it is not surprising that a percentage of cases of classical rheumatoid arthritis exhibits the lupus erythematosus cell phenomenon. It is generally agreed that the diagnosis of lupus erythematosus should not be made in patients with rheumatoid arthritis unless it can be confirmed by other evidence.

Biopsy has been of value in the diagnosis of rheumatoid arthritis. This is particularly indicated in cases of tenosynovitis. The author does not consider the mucin test on synovial fluid of any great value in the diagnosis of rheumatoid disease.

The disadvantage of roentgenography in the diagnosis of rheumatoid disease is the time which may elapse before changes occur. A report from Manchester claims 80 per cent of changes occur within six months of onset. It is essential in all cases of rheumatoid arthritis to roentgenograph the hands and feet, and if negative to repeat the roentgenographic examination at intervals.—*J. N. Ané, M.D.*

Vaughan, B. F. The Nisbet Symposium: Collagen disease. Part III. The radiological changes. *Proc. Coll. Radiologists, Australasia*, Sept., 1958, *2*, 11–16.

The author discusses the roentgenographic changes involving the hands and feet in rheumatoid arthritis, gout, lupus erythematosus and scleroderma. Lung changes have been reported in disseminated lupus erythematosus, and gastrointestinal changes have been described in generalized scleroderma. Roentgenograms of the hands and feet are of considerable assistance in distinguishing rheumatoid arthritis from generalized osteoarthritis. Rheumatoid arthritis also must be differentiated from gout. Generalized osteoarthritis and gout are not diseases due to the degeneration of collagen.

In early rheumatoid arthritis, the first roentgenographic changes consist of osteoporosis. The presence and degree of osteoporosis are difficult to determine in some cases. Osteoporosis does not so frequently occur in males and disappears when the rheumatoid arthritis becomes quiescent. Surface erosions are more reliable findings, but may be difficult to detect in the early case. Later manifestations consist of joint space narrowing and "pocketed erosions."

Fletcher and Rowley estimated that 60 per cent of cases of rheumatoid arthritis show diagnostic changes within three months. Eighty per cent showed changes within six months, but some cases take up to three years to develop erosions. Errors have occurred in labeling "pocketed erosions" without osteoporosis in males as "gouty arthritis." Gout does produce deep cystic erosions, but the first and fifth metatarso- or metacarpophalangeal joints are usually affected.

In Still's disease the changes are similar to those of rheumatoid arthritis with the additional sign of periostitis occurring along the shafts of the metacarpals or phalanges. Still's disease also arrests the growth of

bones which are adjacent to the affected joints. Disseminated lupus erythematosus usually affects adolescents or young female adults. One of the earliest and most common symptoms is arthritis. The Rose and Ball tests may be positive. Since lupus erythematosus cells may be found in some cases of rheumatoid arthritis, the differential diagnosis may be very difficult. Characteristically, the erosions and joint space narrowing may be absent. One must remember that a patient with rheumatoid arthritis can develop disseminated lupus erythematosus and show the characteristic changes of rheumatoid arthritis to an advanced degree.

Scleroderma affects females between the ages of thirty and fifty years. The onset is often with polyarthritis. Skin changes and later gastrointestinal and renal lesions occur. The hands show generalized atrophy of the soft tissues. Following absorption of the soft tissues, the terminal phalanges disappear and calcium is deposited in the pulp space.—*J. N. Ané, M.D.*

Saint, Eric G. The Nisbet Symposium: Collagen disease. Part IV. Discussion. *Proc. Coll. Radiologists, Australasia*, Sept., 1958, *2*, 17–19.

The author agrees with Klemperer that the term "collagen disease" has received an exaggerated popularity which may serve to cover puzzling clinical and anatomic features and may produce confusion. Most diseases involve the connective tissue in one way or another. The author believes that each disease should be referred to individually, even though the demarcation between them is sometimes difficult.

Gout is a purely metabolic disease and should be excluded from the group. Genes are important in the etiology of ankylosing spondylitis and in osteoarthritis, at least in so far as Herberden's nodes are inheritable. The relationship of infection is clear in rheumatic fever and amyloidosis and to a lesser extent in periarteritis nodosa. Dermatomyositis may complicate carcinomatosis and myeloma is one of the most common causes of amyloidosis.

The two important factors which are common to all of the disease are the pathologic involvement of the connective tissue and the suggestion that immunity mechanisms are involved.

Connective tissue has supportive, storage and defense functions. The fibroblasts synthesize collagen. The connective tissues should be considered as a highly integrated biologic system of importance in the defense of the host. The corticosteroids and to a lesser extent the sex hormones are of importance in the modification of specific action.

"Fibrinoid" is seen in all of the diseases of this group. It is not believed to be a specific substance and certainly it is not an altered collagen as it has a different roentgen diffraction pattern and a low hydroxyproline content. Amyloid, which may be found in these diseases, is a mucoprotein substance.

Auto-antibody may be produced against protein derived from central nervous system, skin, liver and blood group substances. There is a possibility that in rheumatoid disease, systemic lupus erythematosus, dermatomyositis, etc., auto-antibody against one or another of the connective tissue proteins is being produced. In rheumatoid disease something in the globulin agglutinates sheep cells. The sensitized cells, the serum polysaccharide, and the specific globulin, all necessary for the precipitin test, might be of help in clearing up aspects of the immunologic problem of rheumatoid disease.—*J. N. Ané, M.D.*

Leger, Lucien, and Guyet, Paulette. (Paris, France.) Lésions kystiques et pseudo-kystiques du pancréas; essai de regroupement à orientation thérapeutique. (Cystic and pseudocystic lesions of the pancreas; proposed reclassification for therapeutic purpose.) *Presse méd.*, Nov. 26, 1958, *66*, 1875–1878.

A reclassification of the cystic lesions of the pancreas as based on nosologic and therapeutic considerations is suggested: (1) exuberant lesions altering the gross morphology of the gland, consisting of true cysts and pseudocysts (necrotic or post-traumatic); (2) intraparenchymal cystic lesions not modifying the contour of the gland and discovered by pancreatography or when a left pancreatectomy is performed, cystic dilatations of Wirsung's canal or interlobular canals, and cystic formations in the parenchyma secondary to canalicular distention or to necrosis.

The authors recognize that such a grouping might appear arbitrary because of the fact that some lesions, well individualized on anatomic and pathogenic grounds, have been reclassified according to their size and their relation to pancreatic canals. For instance, true cysts of small size and without pathologic manifestation are frequently found when a removed pancreatic specimen is examined, and yet they do not produce any apparent deformity. On the other hand, some intraparenchymal postnecrotic cystic cavities seem to be related to the more voluminous pseudocysts.—*Henri-Paul Lévesque, M.D.*

RADIATION THERAPY

del Regato, J. A. Comparación de los resultados de la cirugía con la radioterapía en el tratamiento del carcinoma del cuello del utero. (Comparison of results obtained with surgery and radiation therapy in the treatment of carcinoma of the cervix.) *Radiología, Panamá*, Sept., 1958, *8*, 129–133. (From:

Penrose Cancer Hospital, Colorado Springs, Colo.)

In the last decade advances made in anesthesia and preoperative and postoperative care have enabled surgeons to expand the scope of surgical interventions in the treatment of carcinoma of the cervix. In early stages of the disease, radical hysterectomy with removal of some pelvic lymph nodes has been accomplished with very low mortality rates. In an attempt to improve the curability of cancer of the cervix, the operation has been usually reserved for good risk patients: young, thin women, otherwise in good general condition. In reporting results it has often been customary to compare them with another group of unselected patients treated in the same hospital by means of irradiation only. Because radiation therapy might not have been delivered with the same skill as in other institutions the comparison is not necessarily valid. It may be fruitful to compare, instead, the over-all results of an institution where surgery and irradiation are both used with those of other hospitals where patients receive only radiation therapy. Thus, although Meigs reports 81 per cent five-year survival for Stage I and 59 per cent five-year survival for Stage II in patients operated upon between 1945 and 1950, his *over-all* results for the time period 1944–48 are: 62 per cent five-year survival for Stage I and 45 per cent five-year survival for Stage II. These figures indicate that, on the whole, his patients did not fare as well as those treated in many other hospitals.

In advanced cancer of the cervix the surgical attack involves extensive removal of pelvic organs and tissues, resulting in considerable mortality and great morbidity. It has not yet been proved that the risk and mutilation of these operations are contrabalanced by better survivals. The author compares his 32 per cent five-year survival in Stage III and 15 per cent in Stage IV in unselected patients treated with external irradiation combined with intravaginal radiation therapy with a group of patients reported by Brunschwig showing 17 per cent five-year survival for Stage III and 11 per cent for Stage IV, who had pelvic exenterations.—*F. Comas, M.D.*

Miller, Norman F., Ludovici, Peter P., Christian, Robert T., and Riley, Gardner M. Irradiation sensitivity of cervix cancer; response of cultured cervix cancer cells to irradiation. *Am. J. Obst. & Gynec.*, Nov., 1958, *76*, 1071–1082. (From: The Reuben Peterson Memorial Research Laboratory, Department of Obstetrics and Gynecology, The University of Michigan, Ann Arbor, Mich.)

Irradiation, at present, is our principal therapeutic weapon against cancer of the uterine cervix. In general, the tendency is to administer a dose based on what normal tissue will tolerate, and by so doing hope the cancer is destroyed. Some cancers, however, could be destroyed by a much smaller dose of irradiation, while others will not respond before the adjacent normal tissue is destroyed. These might better be benefited directly at the onset by radical surgery.

Attempts at predicting radiosensitivity have been made on the basis of histologic cancer grading, evaluation of benign vaginal cells, serial tumor biopsies during treatment, and by studying nucleoprotein patterns of tumor cells. The primary purpose of this study was to determine the relative radiosensitivity of patients' cultured cells with the thought that the *in vitro* index of behavior might reflect the tumor's radiation response *in vivo*.

The technique was to obtain preirradiation biopsy specimens of tumor tissue and explant them to the inside glass surface of roller tubes containing appropriate nutrient fluid and incubate them in a roller drum apparatus. Each culture was examined microscopically daily.

Two studies were carried out, with a nonirradiated control being kept for each patient. One was an *in situ* clinical procedure in which the patient's cultured cells were placed in a special container and inserted into the vagina adjacent to the cervix. The culture was thus irradiated at the same time and under the same conditions as the tumor cells. Immediately after treatment the culture was returned to the incubator. The other study consisted of irradiating culture tubes in a pelvic masonite phantom under conditions simulating those received by the patient's tumor cells *in situ*, including exposure to the same daily air dose.

Microscopically, the criterion selected for the end point of the radiation effect was the destruction of *all* outgrowing tumor cells from the culture explant. In both studies there were definite differences in the *in vitro* radiosensitivity of the various tumor cultures. In the absence of five year survival rates for confirmation, a tentative mathematical formula permitting a grading of these differences was proposed. This was $E = (r \times S)/1{,}000$, where E is the tissue culture radiation effect index, r the lethal or total roentgen dose, and S the number of days the culture survived subsequent to the first day of irradiation. The authors have tentatively assumed that values of 0 to 49 represent radiosensitive tumors; 50 to 99 represent tumors with an intermediate radiosensitivity; and 100 or greater represent relatively radioresistant cancers.

Thus, of 24 cases suitable for analysis 8 were classified as resistant, 4 as intermediate and 12 as sensitive. Supporting the tentative classification are reports that of the 8 patients judged as having radioresistant tumors, one died in five months and another developed a recurrence in nine months. Others have shown a clinically satisfactory response up to twenty-

one months. It is of interest that up to now no radioresistant adenocarcinomas of the cervix have been found.

Other factors to be considered in evaluating the prognosis are the extent or stage of the disease and the host resistance. While the clinical extent of the neoplasm can be approximated, there is as yet no satisfactory method for the determination of host resistance.

The results indicate that some carcinomas are relatively resistant to irradiation, whereas others are readily destroyed. Although the results appear promising, it is premature to assume that radiosensitivity of cultured cancer cells *in vitro* truly reflects the tumor's response *in vivo*.—*Donald M. Monson, M.D.*

Jackson, Harvey. (London, England.) Discussion on pituitary tumours; surgical aspects. *Proc. Roy. Soc. Med.*, Nov., 1958, *51*, 907–911.

This is a brief review of pituitary adenomas of the chromophobe, chromophil, and basophil types, and also includes hypophyseal duct tumors or craniopharyngiomas. The author emphasizes the marked variation in the clinical picture of pituitary adenomas and correlates the symptoms with the direction in which the tumor has extended. Any extension outside the sella is of paramount importance because the risks of operation are greatly increased. Hemorrhage into pituitary adenomas is by no means exceptional.

Hypophyseal duct tumors, or craniopharyngiomas, account for about 4 per cent of all intracranial tumors. They may be found either within the sella or above it. Approximately 70 to 80 per cent of these tumors show calcific deposits.

The author believes that progressive involvement, especially of the visual fields, is the main indication for surgery. He does not operate on patients with endocrine disorders alone, and he does not treat tumors which appear to be stable, even though there is a visual field disorder. Where it applies, surgery should be given primary consideration, but a course of radiation therapy should follow. This decision is based on the following: (1) there is an unsatisfactory response to initial radiation therapy in 58 per cent of the cases, according to the series reported by Horrax, (2) craniopharyngiomas and cystic adenomas do not usually respond to irradiation, and (3) high voltage therapy may have disastrous results, but this is presumably avoidable with good technique.

The author concludes that primary irradiation should be reserved for cases where the tumor has escaped beyond the sella, but he does not elaborate on this statement. No statistics are given.—*J. L. Williams, M.D.*

Richmond, J. Jackson. (London, England.) Discussion on pituitary tumours; the role of radiotherapy. *Proc. Roy. Soc. Med.*, Nov., 1958, *51*, 911–914.

In England it is common practice to excise a major portion of pituitary adenomas and then give postoperative irradiation. The advantages are enumerated as follows: (1) the procedure permits immediate decompression of the visual pathways and prevents the appearance or progression of visual difficulties during radiation therapy; (2) the size, extent and histology of the tumor can be determined; (3) excision of a large part of the tumor makes it possible to use small treatment portals postoperatively.

The disadvantage of surgery lies in the operative mortality which fortunately is now low.

Two hundred twenty cases treated with radiation therapy are reviewed. Seventy-five per cent of these were histologically verified chromophobe tumors, 7 per cent were eosinophil tumors, and 5 per cent were craniopharyngiomas. Nine cases of pituitary basophilism and 7 cases of carcinoma of the pituitary gland were treated. Twelve cases were presumably chromophobe adenomas, but were not explored.

Radiation therapy was given through five 4 cm. square fields using a beam with a half value layer of 3 mm. Cu. Currently, the maximum tumor dose is 3,750 r in four weeks (the dose was recently reduced from 4,000 r given in the same period).

Following the combined surgical and radiation treatment, there was some form of visual improvement in 87 per cent of the chromophobe adenomas. In the eosinophil tumors the results of treatment were more difficult to assess and no statistics are given. Eight of the 9 patients with basophil tumors showed some degree of improvement, and in 3 instances the improvement was striking. The response of craniopharyngiomas was decidedly encouraging in some cases, indicating that these tumors are occasionally radiosensitive. Of the 7 patients with carcinoma, 3 had original chromophobe adenomas which became malignant. Two of these patients died from intracranial metastases. In 4 patients the tumors were presumably malignant from the outset. Five year survival rates were: chromophobe adenomas 81 per cent, eosinophil adenomas 89 per cent, pituitary basophilism 75 per cent, craniopharyngiomas 75 per cent, carcinomas 57 per cent, unverified adenomas 60 per cent. In the unsuccessful cases the most common causes of death were recurrent adenomas, extreme hypopituitarism, and postirradiation changes in the brain.—*J. L. Williams, M.D.*

Simpson, S. Leonard. (London, England.) Discussion on pituitary tumours; endocrine aspects. *Proc. Roy. Soc. Med.*, Nov., 1958, *51*, 915–916.

Pituitary adenomas may develop insidiously and remain unrecognized for ten or more years. In

chromophobe adenomas the initial symptoms vary markedly. Patients are often treated for many years for amenorrhea, myxedema, migraine, impotence, weakness, etc., before visual impairment or a lateral skull roentgenogram leads to the correct diagnosis. Pituitary hypofunction as a cause of these variable symptoms can be confirmed by laboratory tests, which are based on a secondary failure of adrenal and thyroid activity.

In acromegaly the initial complaint includes such varied symptoms as hirsutism, migraine, excessive perspiration and impotence. Rapid growth in childhood may be a precursor of acromegaly in later life. There may be progression of the disease even though the fundi and visual fields remain unchanged.

Cortisone, hydrocortisone, and prednisone have made substitution therapy for pituitary hypofunction more comprehensive, and have made surgery of the pituitary gland a much safer procedure. One of these substances is recommended before operation and it should be continued after operation until the need for and amount of a maintenance dose is decided. The author prefers prednisone because its sodium-retaining action is negligible. Cortisone and hydrocortisone have an advantage during the operative period because they can be given parenterally.

Testosterone and thyroid are important adjuncts to prednisone. Testosterone has a valuable and often dramatic effect in pituitary hypofunction. The author states that adrenocorticotrophic hormone (ACTH) is a logical alternative to prednisone and testosterone combined, but it has the disadvantage of daily injections, occasional side reactions, and loss of effectiveness after awhile.

In eosinophil tumors it is desirable to have laboratory aids to help determine the extent of hypersecretion of growth hormone. The author believes that the most reliable test currently available is the plasma insulin level, as measured by the uptake of glucose by the isolated diaphragm of a rat.

The need for surgery or radiation therapy in acromegaly should not be determined solely by encroachment of the fundi and visual fields. Clinical and biologic evidence of progressive pituitary hyperfunction is at least of equal importance now that substitution therapy for any subsequent pituitary hypofunction is on a sound basis.—*J. L. Williams, M.D.*

KUTZ, EUGENE R. Intensive cobalt-60 teletherapy of lung cancer. *Radiology*, Sept., 1958, *71*, 327–335. (Address: Allegheny General Hospital, Pittsburgh 12, Pa.)

During the calendar years 1955 and 1956, of the 189 patients with lung cancer treated by cobalt 60 teletherapy there were 182 who had been followed until November, 1957. Nineteen of the 182 patients had clinical and roentgenographic evidence of carcinoma, but no histologic proof.

The treatment plan varied with the location of the lesion, its size and shape, and size of the patient, employing both fixed beam and rotation techniques. The tumor doses varied from 5,000 to 7,000 r for squamous-cell carcinoma whenever possible. The dose to undifferentiated lesions was reduced to less that 5,000 r because early metastases were encountered so frequently.

Esophagitis seemed to occur more frequently with cobalt 60 teletherapy than with conventional radiation therapy, and although radiation sickness occurred almost as frequently its severity appeared to be less. Skin reactions were practically nonexistent in those lesions which were amenable to rotational therapy. Radiation pneumonitis was one of the most serious complications encountered, occurring from one to six months after treatment is almost every case to a greater or lesser extent. The seriousness of this complication was more dependent upon the volume of tissue treated than it was upon the dosage. Radiation pneumonitis appeared to be a more serious problem than it had been with roentgen rays but this was probably due to the consistently higher doses. From an analysis of the survival statistics in this group of patients and their comparison with those reported by other authors, it seems that better results in the treatment of bronchogenic carcinoma can be obtained with higher energy radiation than with radiation of lower energy.—*Walter H. Jarvis, Jr., M.D.*

LOTT, J. S., and SMITH, IVAN H. Cobalt-60 beam therapy in carcinoma of the esophagus. *Radiology*, Sept., 1958, *71*, 321–326. (Address: J. S. Lott, Victoria Hospital, London, Ontario, Canada.)

The authors report their experience with cobalt 60 beam therapy in carcinoma of the esophagus. Between January, 1952 and December, 1956, a total of 68 cases of carcinoma of the esophagus were referred for opinion and treatment. Thirty-seven cases were treated palliatively, incompletely, or not at all, and are not included in the study. Thirty-one cases were treated radically, for cure. All but 3 cases were proved malignant by biopsy. The disease was apparently confined to the esophagus, with no evidence of extension beyond the esophagus, in 21 of the radically treated cases.

Circumaxial rotation therapy at 95 cm. source-to-tumor distance was used in 4 cases. In the first 27 cases, four, five or six fields were employed at 80 cm. source-to-skin distance. All fields were treated daily. Doses for the fixed beam therapy ranged from 5,500 r in two and one-half weeks to 6,700 r in seven weeks. (The present aim is to deliver 5,500 r to 6,500 r in

four to four and one-half weeks total treatment time.)

The most serious complication connected with radical radiation therapy for carcinoma of the esophagus was mediastinal fistula. This complication occurred in 4 cases. One case of asymptomatic pulmonary fibrosis and 1 of mild stricture were observed. Seven of the 31 patients treated radically are alive and apparently free of disease for periods ranging from one to five years.

Based on their experience, the authors conclude that cobalt 60 beam therapy is a more effective method of managing squamous-cell carcinoma of the esophagus than conventional roentgen therapy.—*Arno W. Sommer, M.D.*

Pierquin, B., Tubiana, M., and Dutreix, J. Étude de 54 cas de cancers de l'oesophage thoracique traités par le bétatron (22 mev.). (A study of 54 cases of carcinoma of the thoracic esophagus treated with the 22 mev. betatron.) *J. de radiol., d'électrol. et de méd. nucléaire*, Nov., 1958, *39*, 725–736. (From: Institut Gustave-Roussy, Villejuif [Seine], France.)

Like all publications by Dutreix and his associates, this review covering the treatment of esophageal carcinoma is a masterpiece dealing with techniques as well as with clinical observations. The article is divided into five parts.

Clinical considerations come first. Here the site of the tumor is fitted into a definite classification. Also, the importance of carefully checking its extension by means of roentgenography, esophagoscopy and bronchoscopy is discussed.

Technical considerations follow. After the clinical evaluation of the patient, a complete treatment plan is outlined. Usually, 4 fields (2 anterior and 2 posterior, opposed in pairs) are so chosen as to embrace the whole esophagus. A light plastic jacket is molded on each patient with the ports of entry marked on it. A set-up of photoelectric cells and computers permits an analysis of the dosage and of the direction of the beam during the entire treatment period. Irradiation is carried out on a five day schedule. The tumor dose is 200 rads daily, or 1,000 rads weekly. Thus in six weeks, 6,000 rads are delivered at the level of the lesion.

The authors then discuss the results. Every detail of the 54 cases treated was carefully analyzed. Three of these patients are well, completely free of symptoms, forty-six to forty-eight months after treatment. The survival varies between three and twenty-six months. An interesting fact is the alleviation of dysphagia, which is obtained characteristically with a dose of 2,000 to 3,000 rads at the lesion, the highest percentage occurring around 2,500 rads. Incidents and accidents during and after roentgen therapy were studied. Perforation of the esophagus, degeneration of the myocardium and a change in the blood picture were frequently encountered.

The fourth part of the article lists the details in the individual cases and the fifth part pays particular attention to the advantage of high energy radiation by increasing the ratio of integral tumor dose to the total integral dose. In comparing with 200 kv. radiation, the integral tumor dose/total integral dose was calculated as 0.16 for a 200 kv. apparatus and 0.29 for the 22 mev. betatron.

In conclusion, the authors state that, with a ten month mean survival rate, their final results with the use of a 22 mev. betatron were nearly comparable to those achieved with conventional roentgen therapy. A slight advantage is attributed to the high energy radiation if one considers the immediate better results obtained. These are explained on the basis of a better distribution of the tumor dose and the absence of radiation sickness so that a greater number of patients reach the level of 2,500 rads, beyond which dysphagia occurs. A dose of 6,000 rads in six weeks constitutes in the greater number of cases a good palliative treatment. Rapid improvement is noted in the patient's functional and general condition. However, excepting in very rare cases, 22 mev. betatron therapy may not be considered as a curative treatment in carcinoma of the esophagus.—*Robert L'Abbe, M.D.*

RADIOISOTOPES

Clarke, K. H., Fairley, Keith D., King, W. E., and Milne, Jean. Radioiodine tracer tests in the diagnosis of hyperthyroidism. *Brit. M. J.*, Dec. 13, 1958, *2*, 1444–1446. (From: The Radioiodine Unit, Royal Melbourne Hospital, Melbourne, Australia.)

The authors have found the twenty-four hour radioiodine thyroid uptake to be of little value in assessing the clinical status of patients with suspected thyroid disease. They have therefore tested a number of other determinations and have selected three which they feel are useful not only in preliminary screening, but in sorting out patients whose findings place them in the borderline area between euthyroidism and hyperthyroidism.

The tests evaluated are the two hour thyroid uptake, the two hour neck/thigh ratio and the forty-eight hour serum precipitable I^{131}. All of these determinations are performed with a single tracer dose of 20 μc of I^{131}, administered orally. Using Geiger counting apparatus, counts were made over the neck and thigh at two hours, and a blood sample was drawn at forty-eight hours for serum precipitable radioiodine determination.

A two hour uptake of over 55 per cent of the administered dose was regarded as indicative of a hyperthyroid state. The standards for the two hour neck/thigh ratio were arbitrary, inasmuch as a pair of counters of different counting rates were employed for simultaneous neck and thigh counting. Twenty-four hour counts were made over the thyroid only if treatment was contemplated, since the authors predicate the size of their treatment dose upon the amount of iodine retained at twenty-four hours.

The forty-eight hour PBI^{131} determination was performed by the trichloroacetic acid precipitation method, and samples were surface-counted with Geiger equipment. A value of greater than 0.5 per per cent of the dose administered per liter of plasma was regarded as indicative of hyperthyroidism.

Results of these three determinations are compared in 96 patients who had clinically been placed in the borderline category and who were considered free from influencing medication. The results are compared with the final disposition of the patient, apparently arrived at by weighing clinical findings plus chemical PBI determinations. Each of the three tests seems more effective in correctly classifying hyperthyroid patients, rather than the euthyroid ones, but accuracy is fairly good throughout in a group difficult to separate by any known laboratory procedure. Some work has been done in this country both on the two hour thyroid uptake and two hour neck/thigh ratio, but they are not widely practiced. The simplicity of these determinations suggests that they are worthy of further study.—*Frederick J. Bonte, M.D.*

Cerviño, José M.; Morató Manaro, Julio; Zaldúa de Delfino, Ema; Maggiolo, Jorge; Navarro, Alfredo; and Sprémolla, F. Insuficiencia tiroidea infantil y tiroides accesorias o aberrantes puestas de manifiesto por el I^{131}. (Infantile thyroid insufficiency and accessory or aberrant thyroid tissue demonstrated by the use of I^{131}.) *An. Fac. de med. de Montevideo*, May-Aug., 1958, *43*, 75–86. (From: Cátedra de Clínica Endocrinológica de la Facultad de Medicina, Montevideo, Uruguay.)

Fifteen cases of thyroid insufficiency, 13 of congenital nature and 2 acquired during infancy, have been studied. One case of a lingual thyroid has also been included. Dosages of 100 μc and one of 300 μc were administered. Thyroid uptakes and urinary excretion determinations were performed followed by scanning of the neck with a collimated scintillation counter placed at about 1 or 2 cm. from the skin. The equipment used in the study is not described.

All of these cases had been diagnosed clinically and treated with thyroid extract for periods of seven to twenty-two years. Treatment was discontinued for one month prior to the I^{131} study.

All of the congenital cases revealed no evidence of functioning thyroid tissue in the normal anatomic areas, but some uptake was elicited in aberrant areas. The case of lingual thyroid revealed no clinical evidence of thyroid insufficiency and a normal I^{131} uptake was obtained in this area.

An interesting case is reported of hypothyroidism following excision of a thyroglossal cyst. This case revealed no areas of I^{131} uptake.

The authors conclude that the age of onset of thyroid insufficiency depends on the quantity and functional capacity of the aberrant tissue and that thyroid extract treatment does not appear to atrophy aberrant tissue.—*Cesar E. Rosa-Perez, M.D.*

Foss, O. P. Paper electrophoresis of I^{131}-labelled serum proteins. *Scandinav. J. Clin. & Lab. Investig.*, 1958, *10*, No. 4, 418–426. (From: The Central Clinical Chemical Laboratory, Ullevål Hospital, Oslo, Norway.)

This study concerns a method of labelling serum proteins with I^{131} and subjecting them to paper electrophoresis, in order to determine quantitatively the separated protein fractions by means of radioautography. The method was developed to avoid the concentration procedure required for electrophoresis of serum proteins if the total protein content is less than 1 gm. per 100 ml. (The present study was made of protein solutions with concentrations greater than 1 gm. per 100 ml.)

The study showed that: (1) the reaction between iodine and protein is irreversible; (2) the most favorable pH for iodination is about 9.3; (3) iodination does not influence the electrophoretic pattern; (4) the serum protein fractions have nearly the same uptake of iodine per gram of protein; (5) elemental iodine does not move during electrophoresis while iodinated proteins do; and (6) electrophoresis of mixtures of isolated serum proteins of known concentration demonstrated that the results with I^{131} radioautography are more accurate than by the usual staining strip method.

The authors will present an application of the above method to more dilute solutions in a future article.—*Charles W. Cooley, M.D.*

Müller, J. H. Erfolgreiche Radiojodtherapie bei zwei Fällen von metastasiertem Schilddrüsenkarzinom. (Successful radioiodine therapy in 2 cases of metastatic thyroid carcinoma.) *Radiol. clin.*, Nov., 1958, *27*, 398–402. (From: Radiologiche Abteilung und Histopathologisches Laboratorium der Uni-

versitäts-Frauenklinik, Kantonsspital, Zürich, Switzerland.)

The author stresses the importance of colloid formation in the thyroid tumor for successful treatment with radioiodine. The case reports of two patients (a woman and a man, thirty-three and thirty-two years old, respectively) are presented. Both underwent total thyroidectomy and were afterwards treated with a total dose of 135 mc and 330 mc of radioiodine. The resulting athyrosis was treated with thyroid medication.

Five years after treatment with I^{131} the patients are alive and without any symptoms. Both became parents of healthy children several years after the application of I^{131}.—*Eckart Schackow, M.D.*

Dent, J. N., and Lynn, W. G. A comparison of the effects of goitrogen on thyroid activity in *Triturus viridescens* and *Desmognathus fuscus*. *Biol. Bull.*, Dec., 1958, *115*, 411–420. (From: Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tenn., Department of Biology, University of Virginia, Charlottesville, Va., and Department of Biology, Catholic University of America, Washington, D. C.)

Specimens of the salamanders *Triturus viridescens* and *Desmognathus fuscus* were treated on alternate days with 0.1 ml. of 1.0 per cent thiourea; others were injected on alternate days with 0.1 ml. of 0.2 per cent potassium perchlorate. Histologic study of thyroid gland tissue of experimental and control animals was performed after thirty and forty-six days of treatment, and measurements of uptake and sixty hour turnover of tracer I^{131} were made on those groups of animals treated for forty-six days.

There was evidence from the histologic studies that the thyroid glands of the control *Desmognathus* salamanders were physiologically active, while those of the *Triturus* controls were relatively inactive.

Both thiourea and potassium perchlorate inhibited thyroid function in *Desmognathus*, as shown by gland hypertrophy and increased cell height, and by considerable diminution in the ability of the thyroid to retain iodine over a period of sixty hours.

In *Triturus* both thiourea and potassium perchlorate produced little or no histologic change in the thyroid tissue examined. Thiourea seemed to have little effect on the ability of the gland to retain iodine, but potassium perchlorate markedly reduced iodine storage capacity, as it did in *Desmognathus*.

A theory is advanced that the low level of thyroid activity evinced by *Triturus* is a part of his mechanism of adaptability to a wide range of temperature and climatic conditions. Experiments are now in progress aimed at testing the effect of TSH administration on iodine metabolism in *Triturus*.

Perhaps the tests were performed at a temperature (19°+ or −1° C.) which requires little metabolic activity from the highly adaptable *Triturus*, but represents the optimal environment for *Desmognathus*, which is known to be far less adaptable.—*Frederick J. Bonte, M.D.*

Walthard, B. (Bern, Switzerland.) Struma maligna. (Struma maligna.) *Radiol. clin.*, Sept., 1958, *27*, 275–293.

It has been demonstrated that in spite of iodine administration for goiter prevention, the frequency of occurrence of nodules in the thyroid gland has not decreased. Increased output of the thyrotropic hormone stimulates the growth of thyroid gland. Produced in surplus, this thyrotropic hormone leads to increased formation of the thyroid hormone. The increase in function of the thyroid gland is associated with a morphologic transformation which may lead to proliferation of the gland, the Basedow-thyroid gland.

When there is insufficient formation of the thyroid hormone, the increase in production of the thyrotropic hormone may provoke a proliferative process leading to a diffuse, then to a nodular enlargement of the thyroid gland; namely, adenomas. The greatest significance of the effect of the thyrotropic hormone on the proliferation of the thyroid gland lies in the deficiency of iodine in foods. It is known that in areas of endemic goiter, the number of malignant thyroid tumors is greater. Therefore, in combatting edemic goiter one also hopes to reduce the number of malignant tumors of the thyroid gland. Adenomas of the thyroid serve as a basis for malignant epithelial thyroid tumors.

The metastasizing adenoma of the thyroid gland is the most differentiated form. Invasion of the adenoma into the connective tissue capsule and even into the veins is not indicative of malignancy, particularly in children, since metastases usually appear in patients after forty years of age. The metastases (first in the lungs and bones) contain more colloid than does the primary tumor. The evolution of the primary and secondary tumors is extremely slow. A diagnostic criterion is the frequently observed pulsation, particularly of the metastatic lesions. A characteristic tumor type is the fast growing struma, first described by Langhans. It is found as a single nodule, seldom multiple. Its malignancy is recognized through the infiltration of tumor tissue into the capsule and veins, rarely into the lymphatics. Metastases occur into the lungs and bones, with rare involvement of the regional lymph nodes. New growths may occur up to twenty years after removal of the

primary tumor. It is suspected that this is not really a recurrence but a newly formed tumor which has developed. The solid or squamous cell carcinoma of the thyroid cannot be differentiated from such a tumor arising from other organs. This tumor forms poorly circumscribed single or multiple nodules, infiltrates diffusely throughout the thyroid gland, and invades the blood and lymph vessels, producing widespread metastases. It has been reported that the incidence of this tumor has decreased from 25 per cent to 10.6 per cent of all malignant thyroid neoplasms since the introduction of iodine prophylaxis.

The large cell adenoma (Hürthle-cell) is characterized by the size of the cells. It is probably produced by a disturbance in secretion in the formation and storage of thyroid globulin without the addition of iodine. The Hürthle cell nodules are usually benign but are potentially malignant, especially in older women. Another group of malignant thyroid is the papilloma. Since the introduction of iodine prophylaxis, the number of papillomas has doubled and now comprises 10 per cent of all malignant thyroid tumors. In the U.S.A., the papillomas are called papillary carcinomas and, as in Switzerland, are found in the younger age patients. The so-called lateral aberrant thyroid carcinomas are now believed to be metastatic deposits from an occult papillary carcinoma of the thyroid. Progress of this tumor is slow and metastases to the lungs occur rarely. The question of malignancy of the solitary adenoma is difficult to assess histologically. The sarcomas occur in various forms and metastasize by the blood stream.

The total picture of malignant tumors of the thyroid gland, since iodine prophylaxis was started twenty years ago, has changed inasmuch as the clear-cut malignant forms have decreased, but the conditional new growths, the large-cell adenomas, and the papillomas have increased in number. The knowledge that in endemic areas an adenoma is potentially a malignant tumor demands that all possible measures be taken to prevent the nodular formations in the thyroid gland. It is suggested that in the endemic areas the iodine in salt be increased from 5 to 10 mg. per cent.—*Samuel Richman, M.D.*

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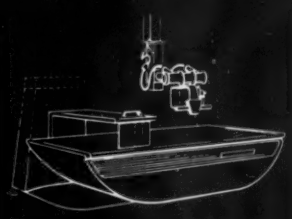

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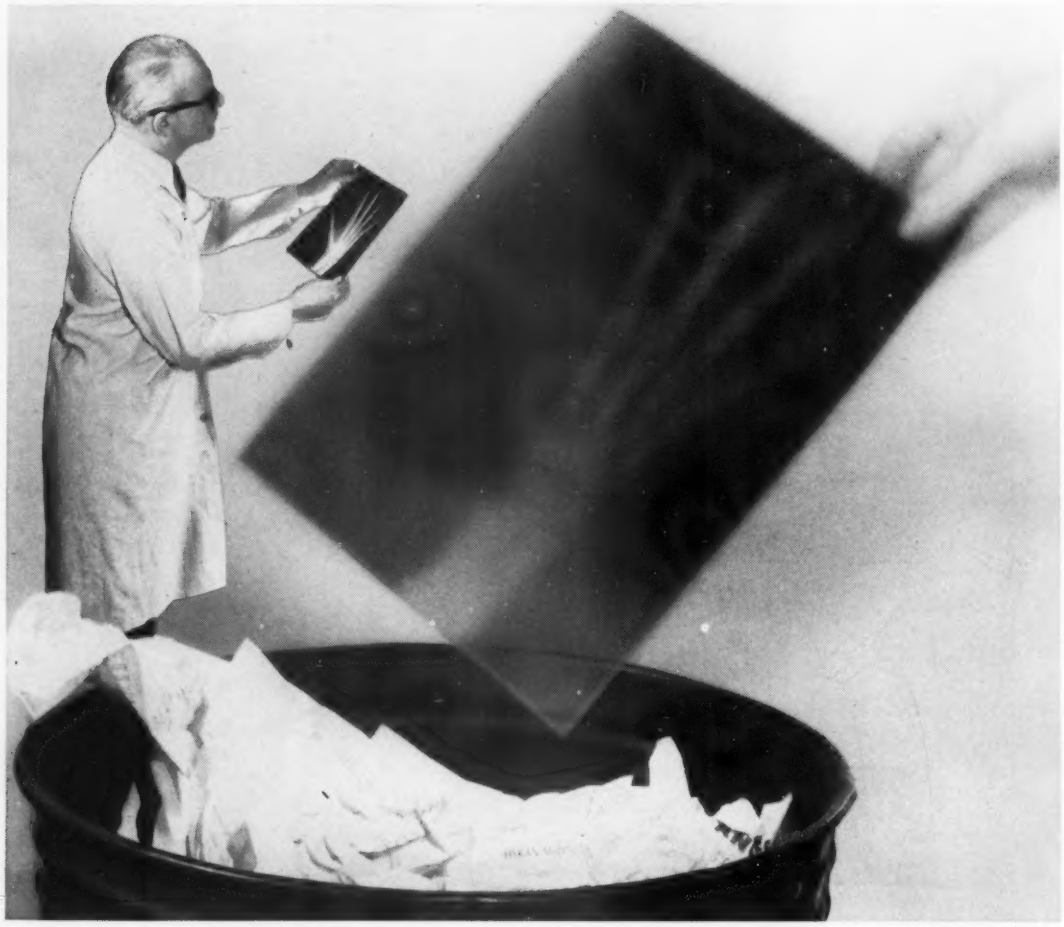

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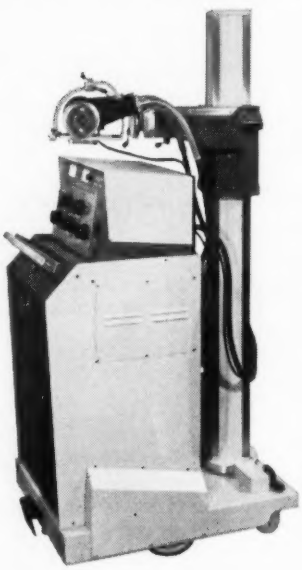

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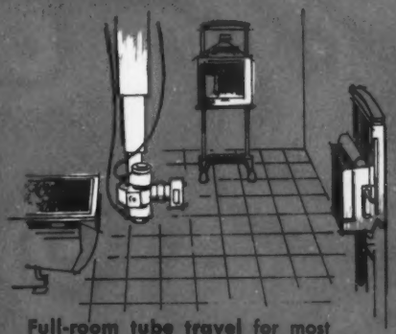

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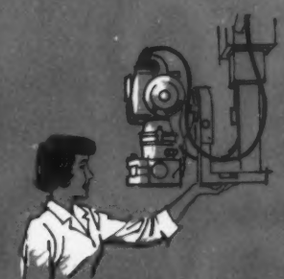

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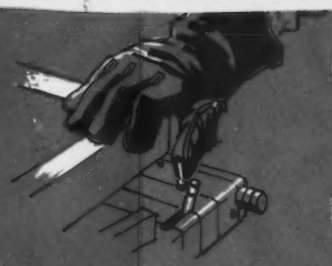

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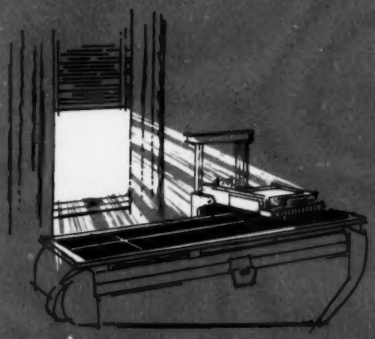

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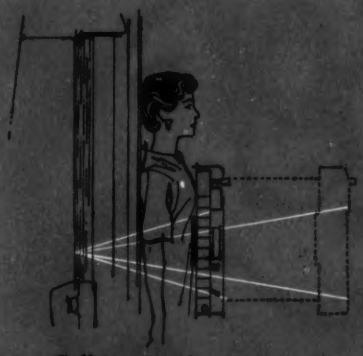

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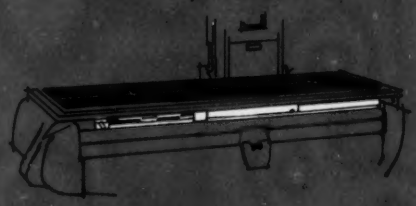

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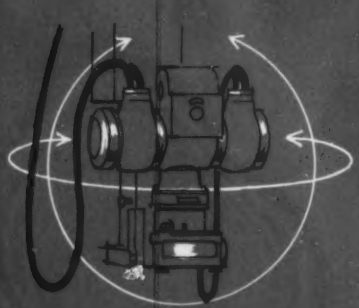

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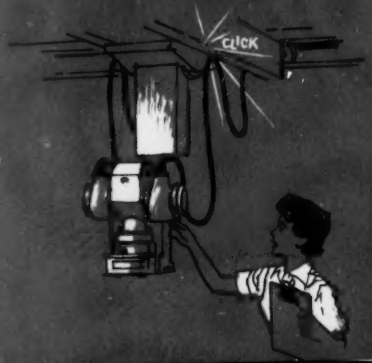

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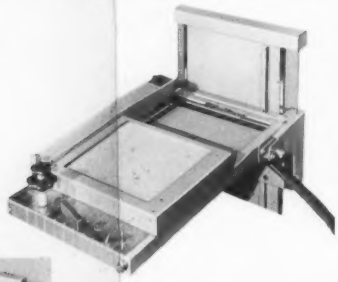
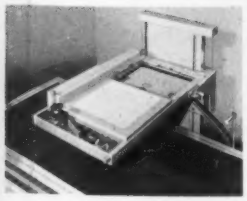
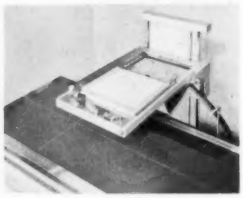
General Electric *lightweight* spot-film units...



MODEL 60-3 automatic, phototimed spot-film device offers power transfer of cassettes *into* and *out of* exposure position . . . many elective exposure patterns. Exposure initiated by pushbutton on spot-film device or by footswitch. Sealed phototiming detector assures consistent film density, exposure after exposure . . . not affected by room light. Cassette ejector pops cassettes well above carriage for easy removal with gloved hand. Convenient, "up-front" controls for film *sequencing, x-ray exposure, cassette release-return, aperture shutters, table tilting, cassette ejection.*



MODEL 60-2 automatic spot-film device — functionally identical to Model 60-3, exclusive of sealed phototiming detector.



MODEL 60-1 semi-automatic spot-film device — performance similar to 60-3 version, exclusive of phototiming. Economical design, employing spring-motor propulsion for fast transfer of cassette to exposure position. Manual cassette return.

You'll like doing business with General Electric

Working with General Electric offers many plus values — extras that cost you nothing, yet count for so much. For one, installation planning — the ability to arrange your equipment for peak functional efficiency. Also nationwide facilities to bring you a complete line of supplies, repair and parts service whenever needed. Technical literature and consultation with skilled engineer-specialists to aid in resolving special x-ray problems.

Still another plus — less apparent but no less significant — is the story told by the G-E nameplate on your apparatus. It's a badge of integrity to patients and professionals alike.

Below is the list of General Electric's cross-country sales offices. Call the one in your locale for complete information on the G-E Regent with new overhead tube hanger. Or write for information to X-Ray Dept., General Electric Company, Milwaukee 1, Wis., Room 1903.

SALES AND SERVICE OFFICES

ALBANY 7, N.Y. - - - - - - 8 Elk St.
ATLANTA 9, GA. - 1383 Spring St., N.W.
BALTIMORE 18, MD. - 3012 Greenmount Ave.
BIRMINGHAM 5, ALA. - - 707 S. 21st St.
BOSTON 35, MASS. - 1256 Soldier Field Rd.
BUFFALO 13, N.Y. - - - 960 Busti Ave.
BUTTE, MONT. - - 103 N. Wyoming St.
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CHARLOTTE 4, N.C. - 1140 Elizabeth Ave.
CHATTONOOGA 3, TENN. - 507 E. Eighth St.
CHICAGO 7, ILL. - 1061 W. Jackson Blvd.
CINCINNATI 25, OHIO - - - - - - - - - - 3056 W. McMicken Ave.
COLUMBUS 12, OHIO - 1373 Grandview Ave.
CLEVELAND 15, OHIO - 3829 Carnegie Ave.
DALLAS 7, TEX. - - 1616 Oaklawn Ave.
DENVER 5, COLO. - - 3031 E. 40th Ave.
DES MOINES 12, IA. - 2211 W. Grand Ave.
DETROIT 19, MICH. - 18801 W. 7 Mile Rd.
DULUTH 1, MINN. - - 928 E. Second St.
EAST SYRACUSE, N.Y. - 1937 Teall Ave.
HARTFORD 5, CONN. - 528 Farmington Ave.
HONOLULU 1, T.H. - Fort and Queen Sts.
HOUSTON 1, TEX. - 1830 Westheimer Rd.
INDIANAPOLIS 7, IND. - 1845 W. 18th St.
JACKSONVILLE, FLA. - - 210 W. 8th St.
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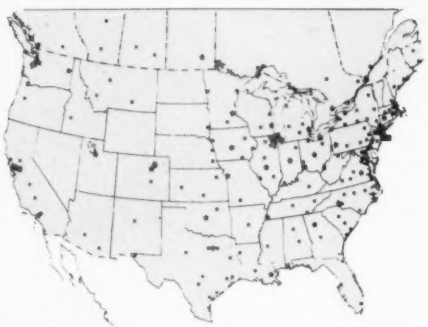
MILWAUKEE 3, WIS. - - 547 N. 16th St.
MINNEAPOLIS 2, MINN. - 808 Nicolett Ave.



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NEW ORLEANS 25, LA. - 7715 Edinburgh St.
NEW YORK 17, N.Y. - - 205 E. 42nd St.
NORFOLK, VA. - - - 218 Flatiron Bldg.
OKLA. CITY 7, OKLA. - 4030 N.W. Tenth St.
OMAHA 2, NEBR. - - 1617 Dodge St.
PHILADELPHIA 32, PA. - - - - - - - - - - Hunting Pk. Ave. at Ridge
PHOENIX, ARIZ. - - 821 W. Adams St.
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PORTLAND 10, ORE. - 522 N.W. 23rd Ave.
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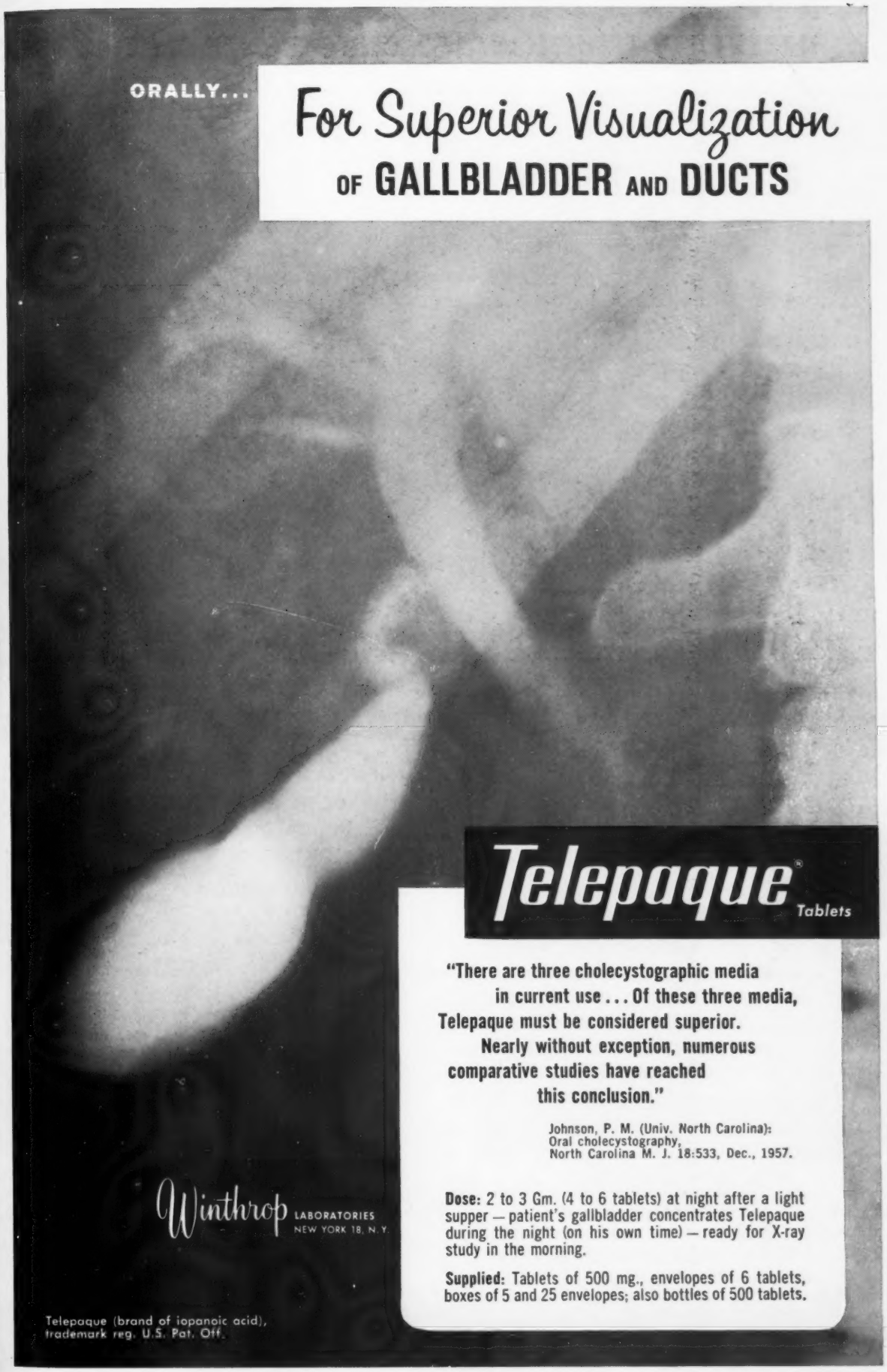

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Johnson, P. M. (Univ. North Carolina):
Oral cholecystography,
North Carolina M. J. 18:533, Dec., 1957.

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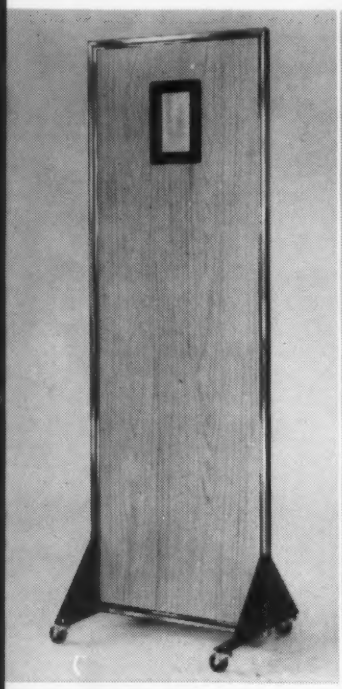

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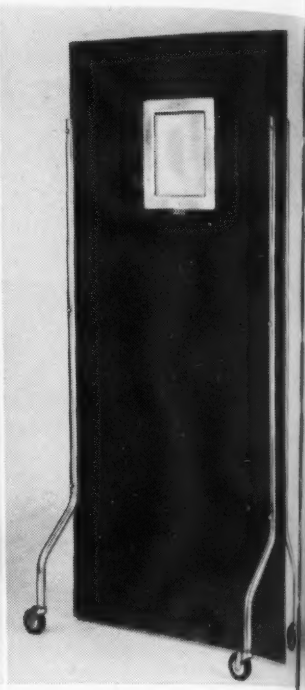

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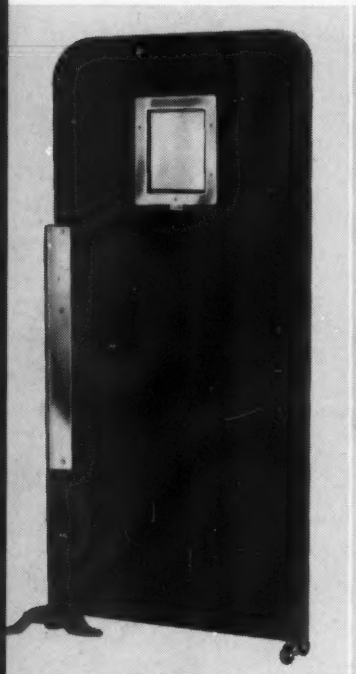

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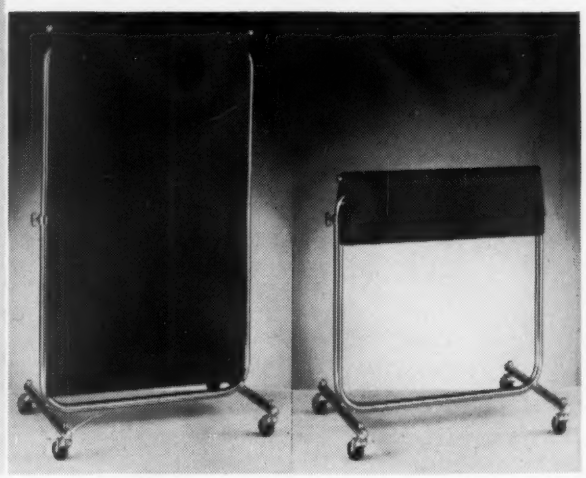

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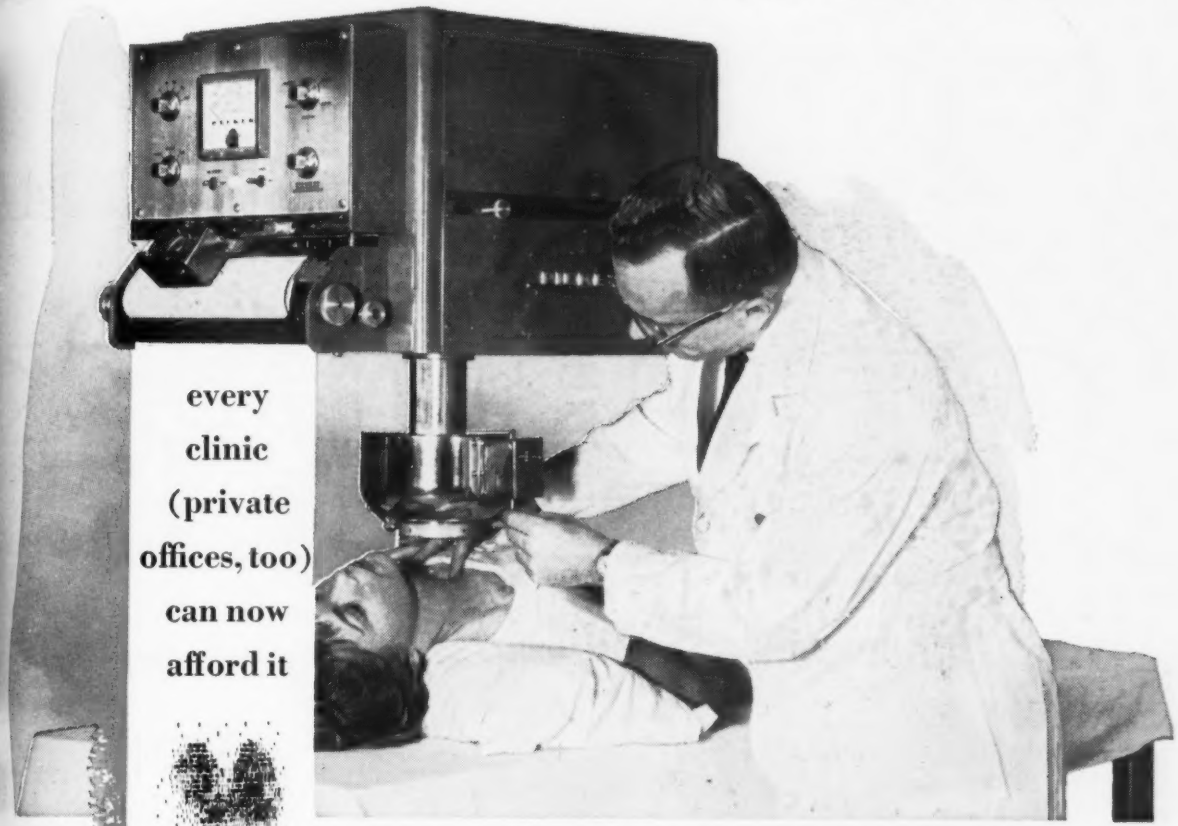

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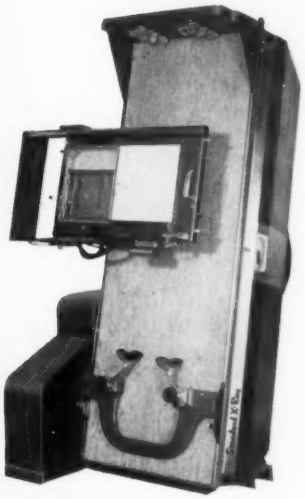

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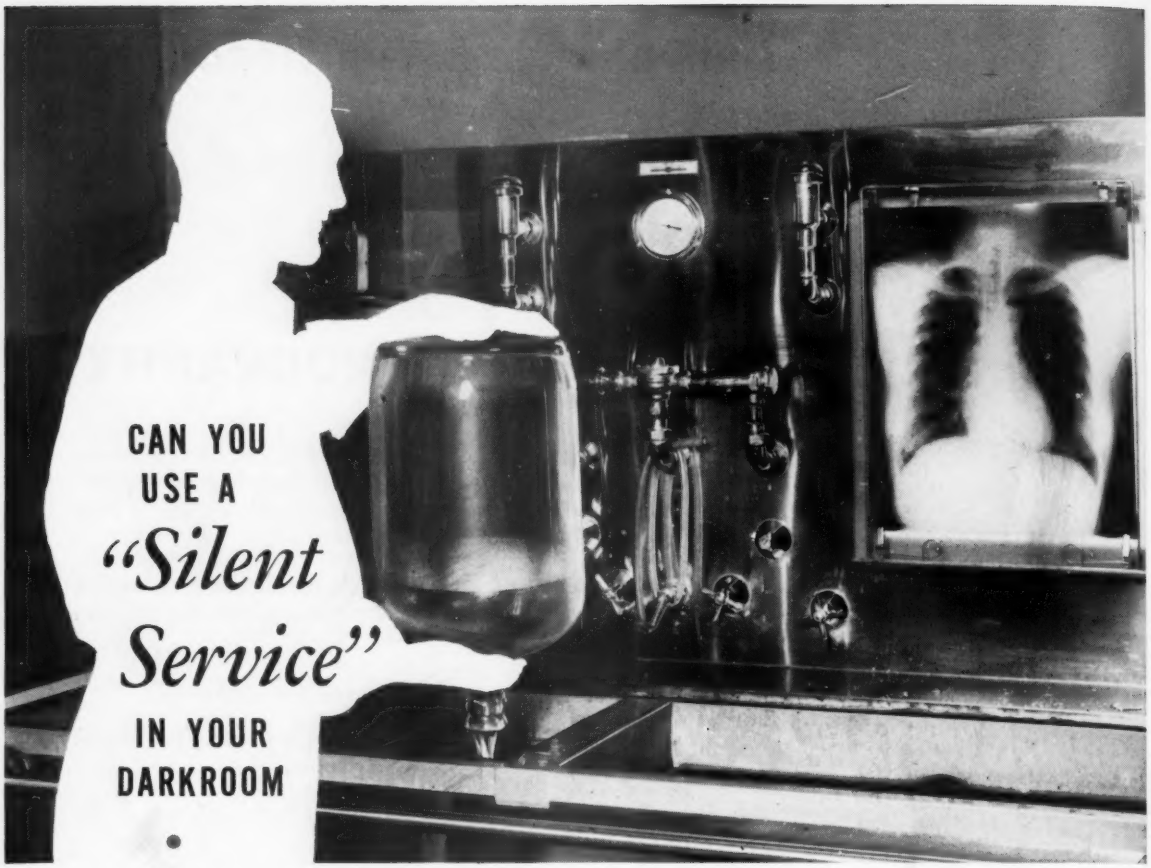

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X-Ray Bulkpak

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. . . try the new **ANSCO BULKPAK**

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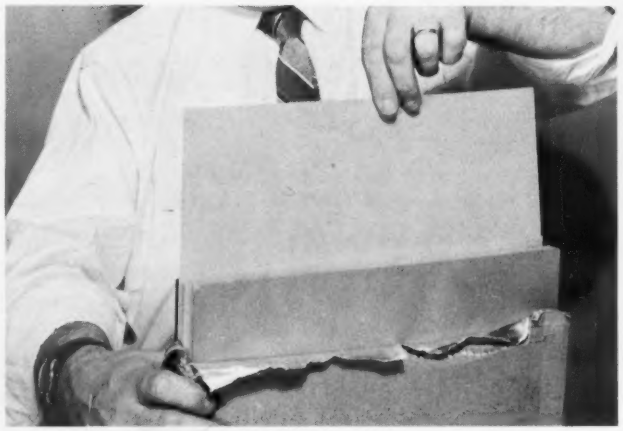

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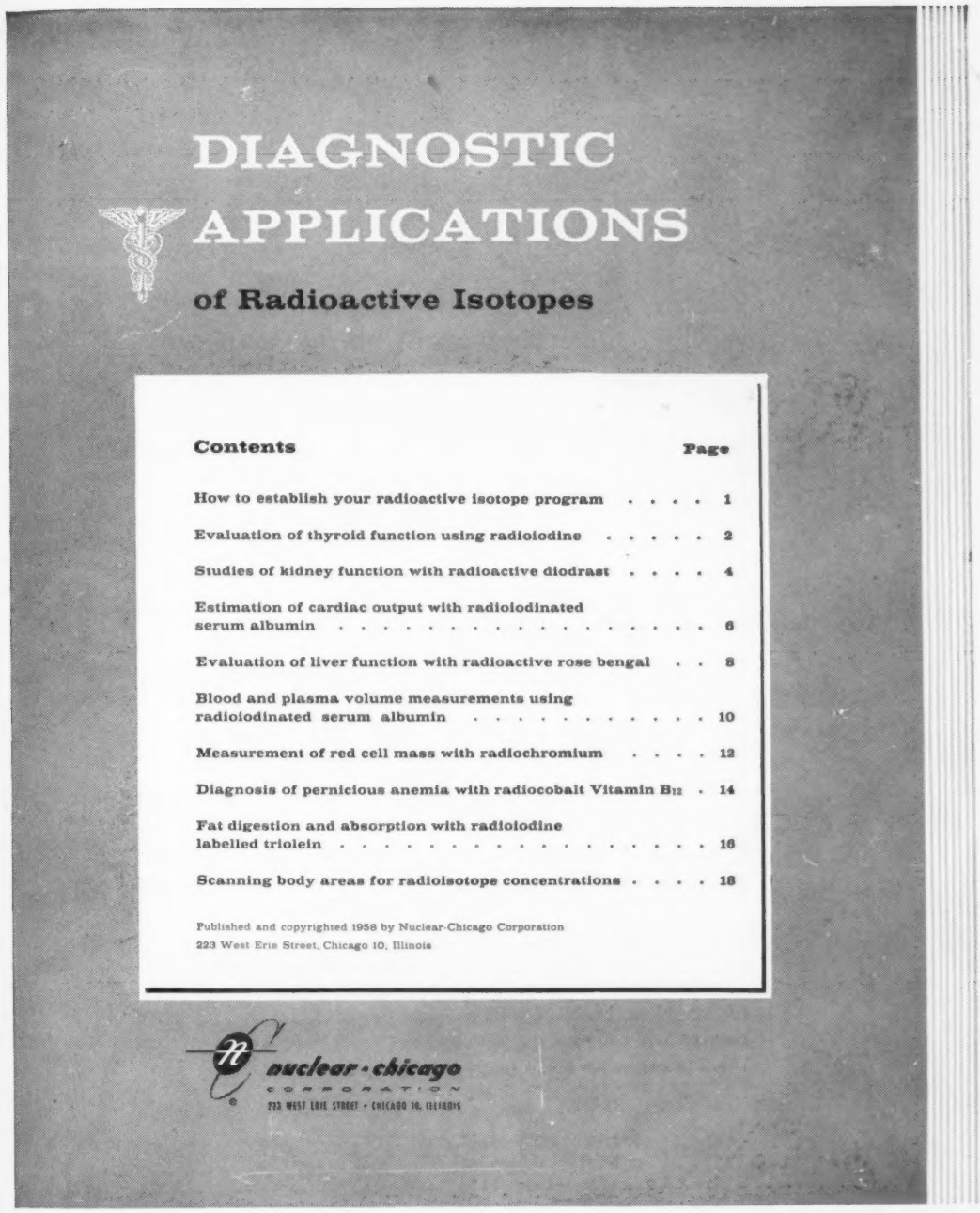
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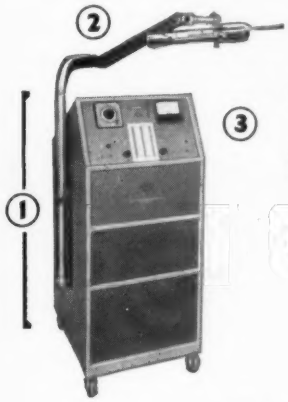

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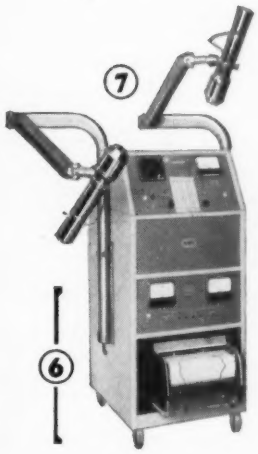

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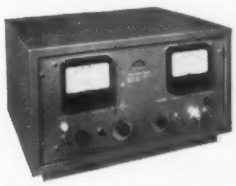

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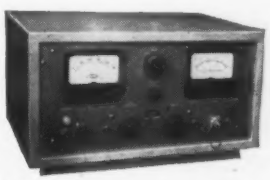

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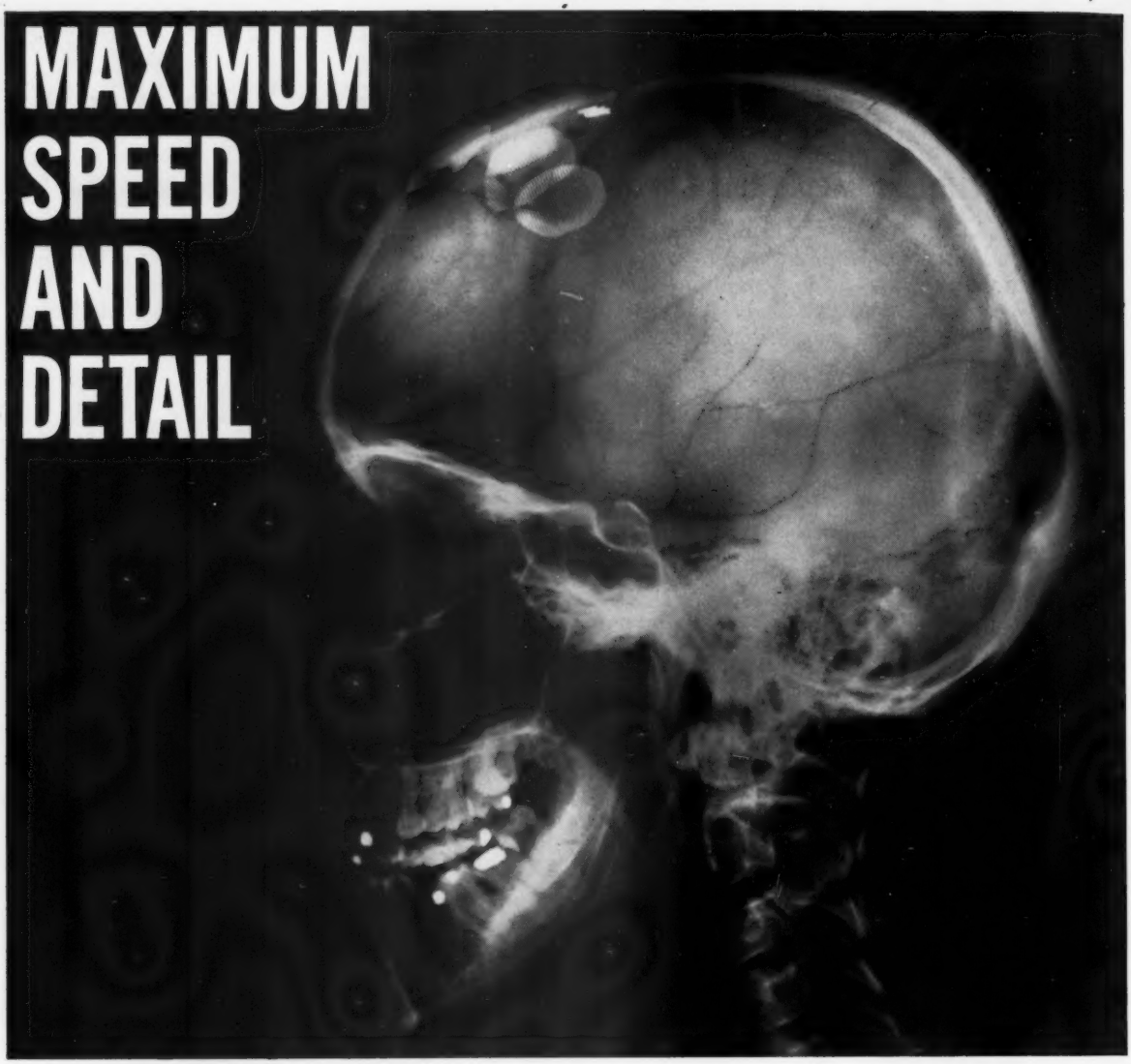

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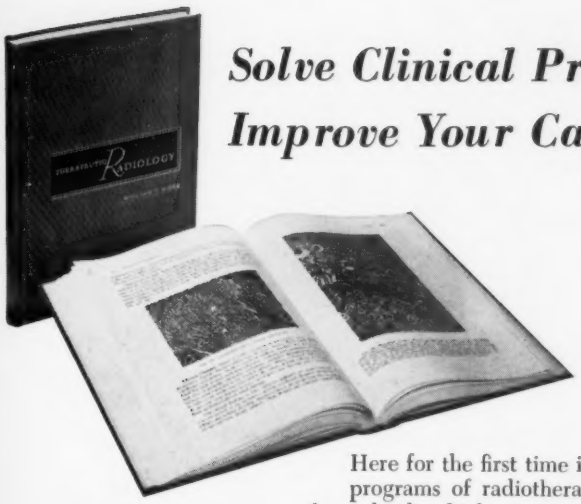

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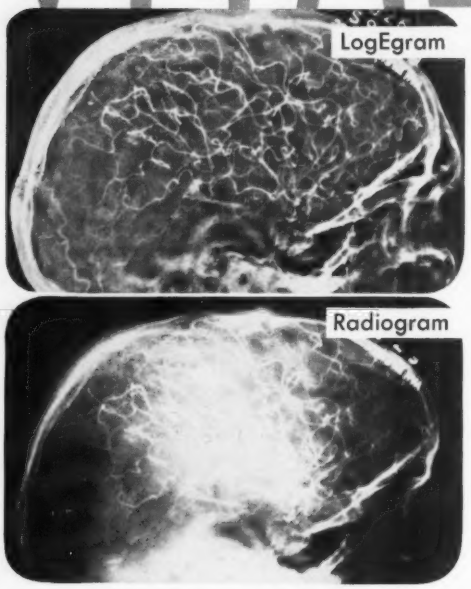

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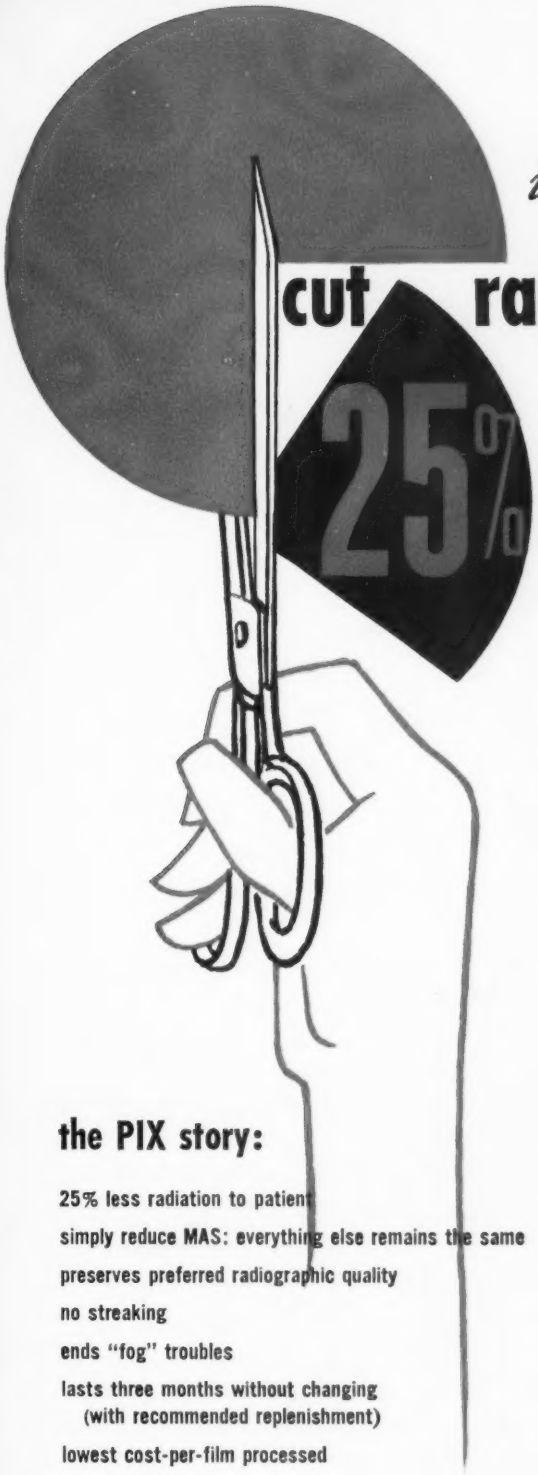

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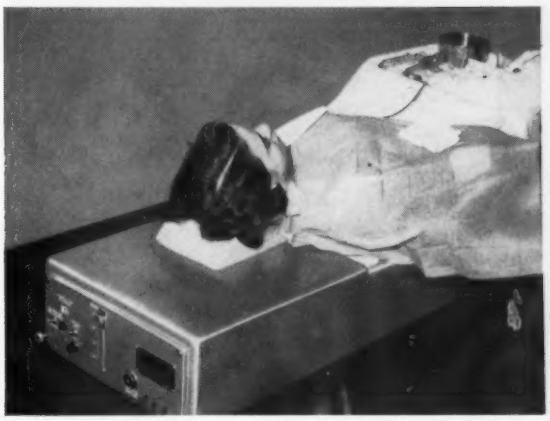

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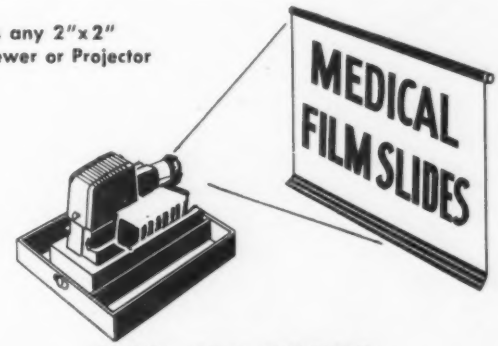

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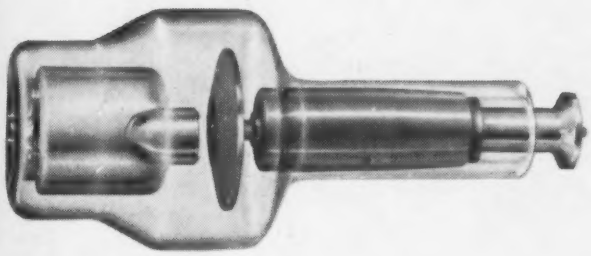

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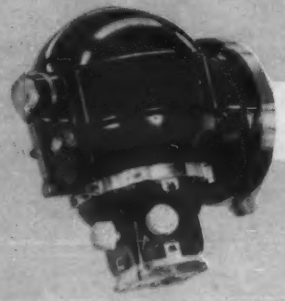

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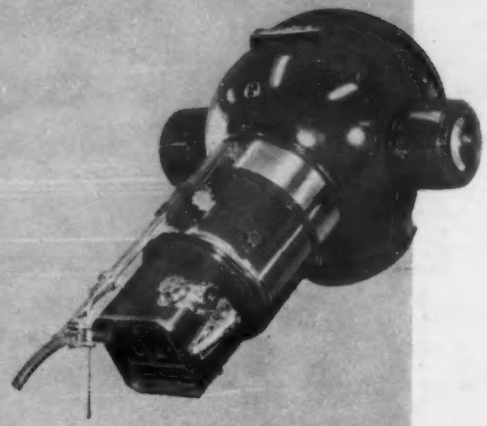

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